11 Paying Attention to a Field in Crisis
Psychiatry, Neuroscience, and Functional Systems of the Brain

Amir Raz and Ethan Macdonald

Introduction

A few short weeks before the long-awaited publication of DSM-5, Thomas Insel, director of the National Institute of Mental Health (NIMH), stated that the manual suffers from a “lack of validity” (Insel, 2013). To remedy this problem, he envisaged a new direction for psychiatry whereby clinicians and researchers classify disorders based on underlying neurobiological causes rather than on highly variable symptoms.

The anticipation of DSM-5 and professional efforts surrounding it generated unprecedented questioning from both consumers and practitioners. The public, advocacy groups, and even senior members of the psychiatric community raised questions, not only regarding decisions to include or exclude specific types of problems from the revised manual but also concerning the scientific foundation of the whole enterprise. Many of these criticisms were based on recognizing the limited advances that have been made in the biological understanding and treatment of mental disorders.

Psychiatry aims to link behavioral science to underlying mechanisms, using the techniques of neuroscience. Yet decades of work on cognitive, molecular, and systems neuroscience have taught most scientists a lesson in humility: despite an enormous investment in research with an emphasis on the neural correlates of typical and atypical behavioral “phenotypes,” breakthroughs are sorely lacking. In spite of the global efforts and the accumulation of a large body of findings, the lack of clinical advances has undermined many working assumptions concerning the neurobiological basis of psychiatric distress.

The genetic and neuroimaging revolutions – which seemed poised to elucidate and ultimately explain conditions categorized as psychopathologies and psychiatric disorders – have produced modest results that speak only obliquely to the vast, complex dynamics revealed by behavioral science. Many scholars are disillusioned with imaging studies of the living human brain, and further recognize that genetic
polymorphisms putatively appearing to increase risk of schizophrenia in one person may actually predispose another to bipolar disorder (Bilder, 2011). Furthermore, some scientists argue that the therapeutic effects of drugs that comprise the backbone of modern psychiatry—antidepressants and atypical antipsychotics—are largely indistinguishable from placebos in common clinical situations (Raz & Harris, in press). These findings challenge the extent to which the study of pharmaceutical drugs contributes to our understanding of psychological conditions.

Neuroscience and biology have given us neither the hoped for refinement of diagnostic criteria nor the sensitivity and specificity required for effective clinical practice. Psychiatry needs an entirely new approach that would allow us to understand—in a tangible way—the diversity of experience in illness and in health. Whereas older models of the DSM represented psychiatric illnesses as categories discontinuous with “normal” functioning, the NIMH strategy with respect to the Research Domain Criteria (RDoC) project emphasizes the potential continuity of psychopathology with normal functioning. For example, RDoC recognizes “attention” as a construct under the “cognitive systems” domain in the belief that examining its underlying mechanisms may account for both everyday behavior and related pathologies, such as ADHD.

Recent neuroimaging studies have clarified some of the neuroanatomical pathways involved in attention networks. Appreciating the challenges cognitive neuroscience faces, as well as the limitations of current techniques, is important in assessing the strength of particular neuroscientific findings and their implications for psychiatry and psychology. Critics have censured cognitive neuroscience for interpreting neuroimaging results in naive ways that amount to a “new phrenology” (Uttal, 2001). These criticisms are justified in many areas of research, where reverse inferences and unsupported assumptions run rampant, as well as in some unscrupulous clinical applications, but they do not invalidate the field as a whole (Raz, 2012). But imaging the living brain and drawing conclusions from the enormous amount of data collected poses both technical and conceptual challenges.

In that spirit, our chapter sketches a new model for psychiatry that draws on recent work in the cognitive neuroscience of attention. We provide a detailed example of how operationalizing psychological and mental terms—in this case, “attention”—as a functional “organ system” (Posner & Fan, 2008) opens avenues to the integration of biobehavioral science and clinical psychiatry and allows us to transcend the old clinical dichotomy of functional and organic (Raz & Wolfson, 2010).
Why Should Psychiatrists Pay Attention to the Scientific Study of Attention?

Attention is a central theme in cognitive science, linking brain with behavior and advancing psychology with the techniques of neuroscience. Although experimental psychology has probably examined the topic of attention more than any other field (Raz & Buhle, 2006), the cognitive neuroscience of attention involves a larger social context that extends far beyond laboratory experiments, with innovative applications to mental health, education, human performance, and many other domains (Posner, 2012a). By understanding attention in terms of the orchestra-
tion of several separate control networks, we can consolidate behavioral, imaging, and genetic findings into a coherent whole. Moreover, we can elucidate individual differences in attention and outline the roles of early experience, upbringing, and environment in the development of attention networks. The scientific study of attention, therefore, provides critical insights into an alternative model that can help reorient psychiatry.

In the following sections, we show how viewing attention as a functional organ system – with its own anatomy, circuitry, and cellular structure – aids in our conceptualization of many psychopathologies. Moreover, we will argue that the pathologies of attention comprise a sizeable domain within the field of psychiatry and provide a way to group problems that transcends traditional diagnostic categories. This approach builds on our knowledge of the evolutionary and developmental bases of a principle brain mechanism of voluntary control, and thus paves the way to a better understanding of how genetics and culture together shape control systems. By studying the unique neurobiological and functional characteristics of brain networks, researchers can systematically search for genetic variations (e.g., polymorphisms) associated with differences in the regulation of cognition, emotion, thought, and action. Identifying this kind of variation can shed considerable light on both typical and atypical behaviors and provide critical insights to psychiatry.

The mapping of the human genome offers the potential to increase understanding of how biology and environment interact to produce individual differences in temperament and other dimensions of human behavior and functioning. Many genes exhibit variations that code for different phenotypes, which, in turn, can alter the efficiency of specific attention networks. The dopamine 4 receptor gene (DRD4), for example, has several versions that differ in having two, four, or seven repeats of a portion of the gene, and these variations may correlate with the temperamental trait of sensation-seeking – the tendency to seek out
novel, varied, and intense sensory experiences (LaHoste et al., 1996). These genetic variations interact with specific aspects of the social environment. Thus, in the presence of the seven-repeat DRD4 variant, parenting has a significant effect on an array of temperamental dimensions that correspond to some of the symptoms found in children diagnosed with ADHD (Sheese, Voelker, Rothbart, & Posner, 2007). Children with the seven-repeat allele who had a lower quality of parenting had unusually high levels of sensation-seeking, including impulsivity. By identifying children who are more susceptible to environmental factors, we can determine which children will benefit most from therapies that aim to improve attention. Hence, genetic variation provides a tool for refining our understanding of environmental influences.

A systematic account of the biological substrates of attention and their relation to social processes can clarify the impact that genetic variation has on each network. For example, experimental studies examining spatial orienting suggest that anxious people orient toward negative and positive targets in a similar manner, but highly anxious individuals have trouble disengaging from the negative target when the cue is invalid (Posner, Walker, Friedrich, & Rafal, 1984). These findings complement data from recent studies showing an inverse correlation between negative affect and effortful control (e.g., Rothbart, 2011). Overall, this research suggests that clinicians may use attention training as a strategy to bolster executive attention and help patients disengage from negative ideation.

The three-network model of attention systems described in this chapter provides researchers and practitioners with tools to examine clinical interventions, rehabilitation programs, educational methods, and even parenting styles. By construing attention as a functional organ system, we focus on its functional connectivity, neuroanatomy, network dynamics, cellular structure, and electrochemical mechanisms. This multilevel integrative view shows the way toward interdisciplinary work unifying the social world, life experiences, biological processes, and computational sciences.

Although attention networks occupy a central place in psychological and cognitive science, they have had relatively limited application in mental health theory and practice. Looking into the past and projecting into the future, attention research may be expected to have a much wider impact. Half a century ago, researchers largely focused on demonstrating that attention changes specific operations in the information-processing hierarchy—from input all the way to behavioral outcome. However, since the 1990s, neuroimaging has increasingly elucidated the focal brain areas that subserve attention networks. Investigators now study the brain regions within these networks that operationalize the computations
performed by attention and monitor their patterns and rhythmic activations in real time. Present since early childhood, attention networks evolve throughout the life span and into adulthood via changes in connectivity (Posner, Rothbart, Sheese, & Voelker, 2014). Although genetic variations interacting with environment give rise to individual differences in the efficiency of control networks that compose attention, recent findings show that practice can improve the operation of specific attention networks by altering overarching brain states (Rabipour & Raz, 2012). Future studies may lead to new methods to ameliorate deficiencies and enhance performance.

Attention as a Functional Organ System: A Metaphor for a New Psychiatry

The notion of attention is part of our everyday “folk psychology.” Titchener (1909) considered attention “the heart of the psychological enterprise”; and William James (1890) contended that, “Everyone knows what attention is. It is the taking possession of the mind in clear and vivid form of one out of what seem several simultaneous objects or trains of thought.” This subjective definition, which construes attention intuitively as a unitary process under voluntary control, bears little resemblance to the working models of attention developed by cognitive neuroscientists (Posner, 2012a), who view attention in terms of a variety of networks that coordinate or facilitate much of human experience and consciousness.

We will outline a view of attention as a set of three distinct networks (alerting, orienting, and executive attention). Overall, we consider “attention” to be a “functional organ system.” According to the OED, an organ “system” refers to “a set of organs or parts in an animal body of the same or similar structure, or subserving the same function,” as exemplified by the digestive system. The term “functional” organ system serves to bridge an outdated dichotomy between “functional” (i.e., psychological) and “organic” (biological) mental disorders (Beer, 1996) that continues to influence clinical thinking (Miresco & Kirmayer, 2006).

Over the last half-century, the three-network model of attention has been continually refined (Posner, 2012a). Although most of the research has focused on visual attention, this approach generalizes across all sensory modalities (Posner, 2012b). Briefly, alerting can be conceptualized as a foundation upon which orienting and executive attention rest. It maintains sensitivity to incoming stimuli. Orienting concerns the selection of information from incoming stimuli. Lastly, executive attention involves complex higher-order processing, including conflict monitoring.
and inhibitory control (Posner & Fan, 2008; Posner & Petersen, 1990). Each network is associated with its own set of physiological activations, neuroanatomical structures, and neuromodulators (see Table 11.1; Posner & Fan, 2008; Rueda, Posner, & Rothbart, 2011).

As neuroimaging studies have shown, a wide variety of cognitive tasks correspond to brain signal changes distributed over a set of neural areas; each of these areas relate to specific mental operations that contribute to the overall cognitive task (Posner & Raichle, 1994, 1998). In the study of attention, the specific neural areas identified have been more consistent than for many other cognitive functions. For example, in order to shift visual attention to a new object, one has to disengage attention from its current focus, move it to the location of the new target, and engage the new object. Many experiments have shown that specific areas of the brain are involved in the operations of disengage (i.e., the parietal lobe), move (i.e., the superior colliculus), and engage (i.e., the pulvinar), and these areas collectively form a functional control system (Posner, 2012b). Together, these loci perform the task of orienting (cf. Losier & Klein,

Table 11.1. Attention Systems Involved in Visual Attention

<table>
<thead>
<tr>
<th>Function</th>
<th>Anatomical Structures</th>
<th>Neuramodulator/Neurotransmitter</th>
<th>Brain Sites</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orienting</td>
<td>Superior parietal</td>
<td>Acetylcholine</td>
<td>A1, V1, S1 (Primary auditory, visual, and somatosensory cortices)</td>
<td>Eye-tracking</td>
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<td></td>
<td>Temporal parietal</td>
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<td></td>
<td>junction</td>
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<td></td>
<td>Frontal eye fields</td>
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<td>Superior colliculus</td>
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<tr>
<td>Alerting</td>
<td>Locus coruleus</td>
<td>Norepinephrine</td>
<td>Orienting system</td>
<td>Autonomic changes, event-related potentials</td>
</tr>
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<td></td>
<td>Right frontal and</td>
<td></td>
<td></td>
<td>Stroop, McGurk, Simon, Go/NoGo, Stop task</td>
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<tr>
<td></td>
<td>parietal cortex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Executive Attention</td>
<td>Anterior cingulate</td>
<td>Dopamine</td>
<td>All over the brain</td>
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<td></td>
<td>Lateral ventral</td>
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<td></td>
<td>Prefrontal</td>
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<tr>
<td></td>
<td>Basal ganglia</td>
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</tbody>
</table>

Brain structures that house the three control networks active in studies of a tripartite broad classification of attention, the corresponding dominant neuromodulators, and the sites of function. Although this illustration focuses on vision, the sources of attention effects appear similar in other modalities (Macaluso, Frith, & Driver, 2000). Adapted from “Attention as an Organ System” by M. J. Posner & J. Fan (2008).
Because attention involves specialized networks to carry out different functions, damage to any module can produce distinct impairments in achieving and maintaining the alert state, orienting to sensory events, or controlling thoughts and feelings (Raz & Buhle, 2006).

Localizing mental operations in separate, yet connected, brain areas suggests a solution to the old problem of how brain localization could occur when widely diffuse damage is observed to produce the same general behavioral effect (e.g., extinction; Karnath & Rorden, 2012). To perform an integrated task, the brain must orchestrate the activity of a distributed network of functionally related anatomical regions; yet, the computations underlying any single mental operation (for example, engagement during orienting, which is orchestrated by the pulvinar) occurs locally. In this view, brain regions coordinate to perform multiple cognitive functions and are not solely defined by the few mental operations ascribed to them in a particular theoretical model or experimental setting (Macdonald & Raz, 2014).

The following sections present evidence for each attentional network and outline their implications for conceptualizing, diagnosing, and treating psychiatric conditions.

**Alerting Attention**

Alerting often appears as a foundational form of attention characterized by individual sensitivity to incoming stimuli, be they visual or other sensory types (Posner, 2012a). In laboratory studies, any stimuli presented to a subject will produce brain activity and physiological arousal compared to the resting state. To separate the activity underlying alerting attention from the resting state, alerting responses are generally measured during the interval between a warning signal and a stimulus. During this period, brain physiology reflects activity suppression, and the parasympathetic nervous system engages as an individual prepares for a swift response to the anticipated stimuli. Alerting increases the efficiency of sensory processing, including processing nontarget stimuli, such as distractors, and influencing orienting and attention networks as needed. Unfortunately, research on the alerting network has been relatively limited, compared with the volume of work on executive and orienting attention networks. As a result, despite the alerting network’s fundamental role in attention, we know less about it.

Anatomically, alerting involves operations in the right frontal and right parietal regions (Posner, 2012a). Evidence in support of this localization includes lesion studies, wherein damage to the right parietal cortex, but not the left, has been associated with diminished alerting capacities.
(Posner, Inhoff, Friedrich, & Cohen, 1987). Recent neuroimaging studies corroborate these findings, showing activity in the parietal and frontal regions during the alert state (Raz & Buhle, 2006). Using a combination of separate modalities, a plausible functional anatomy of the alert state has been posited (Figure 11.1).

The primary neurotransmitter of the alerting network is norepinephrine (NE), which is known to cause widespread effects within the regions that underlie alerting. The source of the brain’s NE pathways, the locus coeruleus, appears to be the substrate for the influence of attention on arousal (Posner, 2012a), and warning signals trigger activity in this area (Aston-Jones & Cohen, 2005). Drugs that reduce or inhibit the release of NE can block the effect of warning signals (Marrocco & Davidson, 1998), whereas NE release enhancers may have the opposite effect (Posner, 2012a). The NE pathway originating in the locus coeruleus connects to regions of the frontal and parietal lobe, where it influences other networks. Studies designed to distinguish between orienting and alerting responses suggest that NE is a primary neuromodulator for the alerting system (Beane & Marrocco, 2004).

Pathologies of alerting due to individual differences in NE modulation have not been directly studied, although other influences on the alerting network have been identified. For example, some people with ADHD and learning disorders have a genetic variation in the alpha-2A receptor gene ADRA2A (Posner, 2012a), which may reflect alertness functioning. Children with ADHD also have increased difficulty maintaining an alert state without a warning signal (Swanson et al., 1991), as well as poorer performance with stimuli presented to the right hemisphere (Posner, 2012a). Of course, some degree of alerting attention is needed for nearly every experimental task of attention. Understanding the bases of individual differences in alerting may allow for more nuanced conceptualizations of cognitive functioning.

**Orienting Attention**

The vast majority of studies on attention have involved orienting to sensory—predominantly visual—events. Orienting, which involves either effortful or reflexive directing of awareness to a stimulus, exists in two major forms: overt and covert. This distinction depends on whether overt physical actions (e.g., eye movements) accompany directing awareness to a new stimulus. Of the three types of attention networks, orienting provides the strongest evidence of mental operations, and researchers usually decompose it into a number of subsidiary processes (e.g., engaging, disengaging, moving). Results from studies since the 1980s,
Figure 11.1 A sketch of the functional anatomy of the attention networks.

The pulvinar, superior colliculus, superior parietal lobe, and frontal eye fields are often activated in studies of the orienting network. The temporoparietal junction is active when a target occurs at a novel location. The anterior cingulate gyrus is an important part of the executive network. Right frontal and parietal areas are active when people maintain the alert state.

including clinical, experimental, and imaging studies, support the
general approach toward localization but suggest somewhat different
decompositions of the operations involved. As new methods of neuroi-
maging have become available, increasingly sophisticated experiments
have been applied to the problem of orienting to sensory input.

Anatomical regions associated with visual orienting include the tem-
poroparietal junction, superior parietal lobe, frontal eye fields, and the
superior colliculus (Posner, 2012a). A paradox of lesion studies in the
early 1980s was that the superior parietal lobe seemed to be the area most
related to producing difficulty in disengaging from a current focus of
attention. Yet, most clinical data point to inferior lesions in the tempor-
oparietal junction and/or the superior temporal lobe to account for
neurological “extinction”; that is, when simultaneously stimulated on
either side of a perceptual field, the patient only perceives stimulus on
one side – even if the patient can identify both stimuli when presented
separately (Vuilleumier & Rafal, 2000). Event-related imaging studies
have served to reconcile this difference. We now know that lesions in two
separate regions in a hemisphere can produce difficulty in shifting atten-
tion to stimuli in the contralateral visual field, but for quite different
reasons. Lesions of the temporoparietal junction or superior temporal
lobe are important when a novel or unexpected stimulus occurs. When
functioning normally, this area allows disengagement from a current
focus of attention in order to shift to the new event. It also plays a critical
role in producing the core elements of the hemispatial neglect syndrome
(or extinction), in which a person becomes unaware of or inattentive to
sensations and events on one side of the body. In addition, considerable
clinical evidence suggests that in humans, lateralization in the right-
temporal parietal junction may be more important to the deficit than
lateralization in corresponding areas of the left hemisphere (Mesulam,
1981; Perry & Zeki, 2000). A different brain region, the superior parietal
lobe (SPL), appears critical for voluntary shifts of attention following a
cue. Event-related functional magnetic resonance (fMRI) studies have
found this region to be active following a cue that informs the person
to shift attention covertly (i.e., without eye movement) to the target
(Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000). The SPL is
part of a larger network that includes frontal eye fields and the superior
colliculus; this network appears to orchestrate both covert shifts of atten-
tion and eye movements toward targets (Corbetta, 1998). During visual
search – when people voluntarily move their attention from location to
location while searching for a visual target – the SPL is also active. By
linking the findings of lesion studies with converging evidence from
event-related imaging studies, research on orienting has identified a
network of behavioral and anatomical features collectively responsible for the movement of attention in either a covert or overt manner (Figure 11.1 and 11.2).

Further distinctions between covert and overt orienting have been posited at a cellular level (Posner, 2012a). For instance, a specific type of neuron seems to be involved in covert shifts of attention (Schafer & Moore, 2007; Thompson, Biscoe, & Sato, 2005), which also continues to attend to, or hold, the locations of cues during delay intervals (Armstrong, Chang, & Moore, 2009). Thus, cellular differentiation contributes to the distinction between motor systems involved in saccades and circuits involved in covert orienting.

Cholinergic systems play a vital role in orienting attention. Even in cases where NE release, and therefore warning signals, cannot occur, orienting can still take place (Marrocco & Davidson, 1998). Studies in monkeys have utilized the acetylcholine (ACh) blocker, scopolamine (which slows covert orienting), to elucidate the role of ACh in orienting (Davidson & Marrocco, 2000). These findings further point to differences in neurotransmitters between alerting and orienting systems.

Abnormalities in the orienting network may contribute to neuropsychological conditions. For example, Alzheimer’s patients with degeneration in the superior parietal lobe have difficulty dealing with cues in the central visual field that are meant to inform them to shift their attention (Parasuraman, Greenwood, Haxby, & Grady, 1992). In addition, of the two main pathways that process visual information in the brain, the ventral information-processing stream represents the “what” stream, which seems to identify objects rather than locate them in space. Patients with lesions of the thalamus (e.g., the pulvinar) show subtle deficits in visual-orienting tasks that are likely related to the ventral information-processing stream. It seems plausible, therefore, that a critical element of orienting would be a vertical network of brain areas related to voluntary eye movements and to processing novel input, but a precise model that includes a role for all visual areas implicated in orienting is still lacking.

The methods of neuroimaging have proven useful in testing the general proposition that mental operations involved in a given task are distributed across multiple brain areas (Posner & Raichle, 1998). Nearly two decades of work have shown many tasks to be associated with the activation of widely spaced networks that are presumed to carry out particular operations. We are still unsure as to the exact operations that occur at each location, even in a relatively simple act such as shifting attention to a novel event. However, imaging data link clinical observations with experimental results to support the general idea of localization of specific operations.
Figure 11.2 Cross-sectional views of the three attention networks.
The alerting network shows thalamic activation, the orienting network shows parietal activation, and the conflict network shows anterior cingulate cortex activation. The color bar shows fMRI signal level (Z-scores) above the 0.05 significance threshold. fMRI images collected from 16 healthy adults performing the ANT in a 3 Tesla MRI scanner (Fan et al., 2001). Reprinted from NeuroImage, 26, J. Fan, B. D. McCandliss, J. Fossella, J. I. Flombaum, & M. I. Posner, “The activation of attentional networks,” p. 476, Copyright 2005, with permission from Elsevier.
Executive Attention

The executive attention network is perhaps the most multifaceted of the functional systems of attention, involving the neural processing required for resolution of conflicts, monitoring, and self-regulation. Common tests of executive attention generally include perceptual conflicts or higher-level brain processing (e.g., Stroop or visual search tasks), and performance on such tasks of executive attention has proven amenable to top-down modulation (Lifshitz, Aubert Bonn, Fischer, Kashem, & Raz, 2012) and cognitive training (Rabipour & Raz, 2012). Moreover, cognitive training programs aimed at strengthening executive attention networks have been found to increase intelligence and self-regulation scores in children (Rueda, Checa, & Santonja, 2008). Although this network has long been associated with the handling of sensory conflicts, recent findings now illuminate the wide-reaching implications of executive attention in self-regulation.

The executive attention network, while interacting with other forms of attention, is anatomically distinct. Exploration of brain activity in the cingulate during tasks of conflict resolution (Pardo, Pardo, Janer, & Raichle, 1990; Posner, 2012a) led to the discovery of the network. In conflict paradigms, including Stroop tasks, the anterior cingulate cortex (ACC) becomes active and contributes to a dynamic process of conflict monitoring and top-down control with the dorsolateral prefrontal cortex (MacDonald, Cohen, Stenger, & Carter, 2000). Utilization of modified Stroop paradigms has further illuminated a distinction between emotional and cognitive areas of the ACC (Bush et al., 1998) – a discovery that has implications for executive control of cognitive and emotional impulses. The major areas of executive attention interface with functionally adjacent brain areas, while maintaining their autonomy as a distinct network (Figure 11.1 and Figure 11.2).

Areas of the executive attention network exhibit particular cell morphologies that provide clues regarding function. Spindle cells are found in areas of the ACC and anterior insula that are unique to great apes and humans (Posner, 2012a). Their presence, as well as the time course of their development, suggest higher cortical functioning concurrent with the development of executive attention. Of course, these cells are not necessarily the same ones that are active during fMRI scans, but further investigation into the function of these cells might provide key insights.

As behavioral genetics advances, novel research paradigms have begun to unravel relationships between genes and executive attention. For example, DRD4 and MAOA polymorphisms, selected for study because
of the importance of dopaminergic pathways in executive attention, have been correlated with performance on an attention network test, and alleles have been identified that correlate both with increased ACC activity and enhanced conflict resolution (Fan, Fossella, Sommer, Wu, & Posner, 2003). Studies of such genetic variation, while in their infancy, will lead to better understanding of the complex gene-brain-environment interactions during development that contribute to cognitive functioning.

Critically important in psychiatric disorders, executive attention has been implicated in a wide range of disorders, including borderline personality and schizophrenia (Posner, 2012a). Such transdiagnostic approaches, congruent with the advent of the RDoC, may prove essential to the development of a scientific basis for psychiatry that is grounded in cognitive neuroscience.

The Functional Anatomy and Genetics of Attention Systems

In summary, recent research has mapped the functional anatomy of multiple systems in the brain. Event-related fMRI studies have identified brain areas or networks associated with alerting, orienting, and executive attention (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). Research on the effects of warning signals (e.g., alerting or expectation of when a target will occur) have shown that, while sustained vigilance involves mainly areas of the right cerebral hemisphere, phasic changes in alertness following warning signals tend to operate through left hemisphere sites (Coull, Nobre, & Frith, 2001). Event-related fMRI studies of orienting (cf. Corbetta & Shulman, 2002) identify a dorsal system that includes the interparietal sulcus and frontal eye fields as key sites triggered by volitional shifts of attention. A more ventral parietal-frontal network serves as a “circuit breaker” leading to shifts of attention, particularly to novel stimuli. The more ventral system has been identified as a major site where cortical lesions produce attentional neglect. There is considerable agreement on which cortical areas orchestrate shifts of attention toward sensory information, but the subcortical areas are still largely unclear (Posner, 2004; Posner, 2012a).

Much effort has been given to determining the exact role of specific areas, including the ACC and lateral prefrontal cortex. Several researchers have argued that the cingulate involves a monitoring function, whereas lateral prefrontal areas act more directly to suppress neural activity in unselected areas (e.g., Cohen, Aston-Jones, & Gilzenrat, 2004). Although consensus on the sites involved in executive attention
exists, active debates continue on whether these brain areas operate as a whole or via local, specific operations (Posner, 2004, Posner, 2012a).

Initial work on the molecular genetics of attention provided evidence on the roles that MAOA, COMT, DRD4, and DAT1 genes play in measures of attention control (Fossella et al., 2002), and major studies from a large group at NIH have confirmed the role of COMT in attention (Blasi et al., 2005). In addition, researchers have identified two cholinergic genes that influence individual differences in the orienting network (Parasuraman, Greenwood, Kumar, & Fossella, 2005). Neuroimaging has been used to further explore the anatomy of these genetic differences (Egan et al., 2003; Fan et al., 2003). The area of cognitive genetics has become a large field, allowing the study of individual differences in attention at the molecular level (Goldberg & Weinberger, 2004). As findings from this field accumulate, we may soon have refined biological correlates of psychiatric distress that can guide the development of clinical interventions based on cultivating our attentional capacities.

**Neurodevelopment of Attention**

The field of developmental cognitive neuroscience has traced the development of the attention systems in some detail (e.g., Posner, 2012a; Posner, Rothbart, Sheese, & Voelker, 2014; Rothbart, Posner, & Kieras, 2006). Not only is this field of particular importance for understanding neurodevelopmental disorders such as ADHD, but it also sheds light on the impact of environmental factors on attention (Posner, 2012a).

In adults, most cognitive and emotional self-regulation involves a network of brain regions drawing on structures such as the ACC, the insula, and areas of the basal ganglia related to executive attention. During infancy and throughout early development, however, control systems depend primarily on a brain network involved in orienting to sensory events that includes areas of the parietal lobe and frontal eye fields (Posner, 2012a).

Over the first few years of life, emotion regulation is a major aspect of development. fMRI studies on newborns and infants up to a year old (Gao et al., 2009), as well as on children and adolescents (Fair et al., 2009; Fair, Dosenbach, Petersen, & Schlaggar, 2012; Fransson et al., 2007), have provided data on two attention networks related to control systems: the frontoparietal network and the cingulo-opercular network. During early development the two networks cooperate closely together, while in adulthood the cingulo-opercular network becomes independent from the frontoparietal network. Drawing on the neural substrates of
the orienting network, the frontoparietal network is important for rapid adaptive control on shorter timescales, whereas the cingulo-opercular network draws on the executive network’s neural infrastructure to maintain stable attentional sets over longer timescales.

These patterns of connectivity suggest that the control structures involved in executive attention – including structures on the medial aspect of the frontal lobe (e.g., ACC) and parietal lobe (e.g., operculum) – are active during early development, maturing to wield fuller control only later in life. The parallels identified by studies of brain networks of attention in adults (e.g., Posner & Fan, 2008) and developmental studies of resting fMRI connectivity (e.g., Fair et al., 2009; Fair et al., 2012) may help unravel the story of the development of attention in infants and young children.

Researchers, including Posner and others, have pursued the study of changes in control in early life, from orienting to executive attention, showing increased frontoparietal (i.e., orienting) resting network activity and reduced cingulo-cuneus (i.e., executive) activity during infancy (Posner, Rothbart, Sheese, & Voelker, 2012). As children develop, executive functioning increases, as indexed by both behavioral measures and neural correlates.

During infancy, orienting serves as the primary control system; later in childhood, effortful control becomes dominant. Control during infancy may be mainly in relation to emotion and only later related to executive functioning. Parents and caregivers probably propel the development of self-regulation and exercise executive systems by presenting novel stimuli (e.g., new objects or people). Reading to the child may be another form of this type of stimulation. Some cultures make “active watching” (e.g., observation and imitation) the main learning venue of the developing young. “High motivation to learn” among the children of Aka and Bofi foragers in the Congo Basin rainforest “occurs early and often. Infants climb into their parents’ laps to watch them cook, play an instrument or make a net” (B. S. Hewlett, Fouts, Boyette, & B. L Hewlett, 2011). Such cultures may prepare the executive attention network of infants by orienting to novel stimuli. The cingulate system appears to function, at least for the detection of errors, as early as seven months of age (Berger, Tzur, & Posner, 2006; cf. Ketay, Aron, & Hedden, 2009; Boduroglu et al., 2009); with epigenetic and environmental interactions shaping the development of the networks in later life (Sheese et al., 2007; Voelker, Sheese, Rothbart, & Posner, 2009), training can increase the efficiency of white matter connections, even in adults (Tang et al., 2010). Therefore, assuming that infants and adults share similar mechanisms with regard to novelty, cingulate activity may forge connections found in
later life. Better understanding of the development of attention systems will have implications for child-rearing, pedagogy, and treating attention-related disorders.

Attention Training: Meditation and Hypnosis

Learning shapes attention systems well into adulthood. Attentional capacities are malleable, and attention can be trained in a number of ways. Michael Posner and colleagues, for example, have tried to distinguish attention training (e.g., conflict-related tasks) from attention state training (e.g., meditative practices accompanied by changes in mind/body states; 2009). Furthermore, they have demonstrated alterations in white matter connectivity in critical areas related to the ACC after attention state training (Tang et al., 2010). Attention state training can improve attention performance and response to stress, and measures of attention have been used with individuals as young as four years old.

The potential clinical value of forms of attentional training such as meditation and hypnosis is apparent from research on pain regulation (Holroyd, 1996); modulation of the immune system (Kiecolt-Glaser, Marucha, Atkinson, & Glaser, 2001); and treatment effectiveness (Kirsch, Montgomery, & Sapirstein, 1995).

Clinical hypnosis involves the deliberate use of attentional capacities to manage symptoms, change behaviors, and produce other helpful outcomes (Nash & Barnier, 2012). During a hypnotherapy session, a therapist uses suggestion in the form of hypnotic instruction to bring about such outcomes in a client. Individuals vary widely in their ability to respond to hypnotic instructions and suggestions. We can measure this individual trait, which is known as hypnotizability, via the use of scales; but no biological marker currently exists for indexing either hypnotizability or the hypnotic experience. In other words, neither a brain scan nor a blood test can determine if a person is highly hypnotizable or if someone is currently experiencing hypnotically induced alterations or effects. In fact, most children are highly hypnotizable, with an age peak of about eleven to twelve years, but hypnotizability seems to gradually diminish for many people thereafter; and adult hypnotizability is a relatively stable characteristic that is normally distributed in the population (Kohen & Olness, 2011; Raz, 2012). A few studies, however, have found that individuals can increase their hypnotic responsiveness through training (Gorassini et al., 1999). Although it is controversial, hypnotizability training aims to teach individuals to direct their attention in a specific fashion to achieve a hypnotic experience (Spanos et al., 1989; cf. Rabipour & Raz, 2012). Although critics argue that the observed
responses may result from a combination of factors, including training-to-task and a certain measure of theatrics and self-deception, little research has examined hypnotic training in depth. It would be interesting to know, for example, whether people with low hypnotizability who undergo training can achieve the ability of highly hypnotizable but untrained people to override automatic effects such as those measured by executive tasks (Lifshitz et al., 2013). Attention training is a form of cognitive intervention, similar to hypnotic training, that is aimed at exercising specific control networks (Rabipour & Raz, 2012). Behavioral programs, including attention training, have become ubiquitous; proponents claim that they can be valuable adjuncts, if not rivals, to conventional pharmacotherapy for certain disorders (e.g., Tourette syndrome), especially in children (Piacentini et al., 2010; Steeves et al., 2012). Finding nondrug treatments for mental and neurological disorders might help patients avoid or limit the side effects of medication; however, this nascent field is still in its infancy (cf Rabipour & Raz, 2012).

Tourette Syndrome: Intervening through the Functional System of Attention

Tourette syndrome (TS) is a neuropsychiatric condition marked by compulsive, habitual movements and vocalizations. Individuals with TS frequently report that these tics are preceded by physical sensations or urges to tic. These proceeding sensations and urges, known as premonitory urges, resemble the sensations and desires to blink that one may get when holding their eyes open for too long. Researchers often consider premonitory urges to be “semivoluntary” since, as with blinking, they can be suppressed only with a great deal of effort and discomfort. Moreover, many individuals with TS find that their tics ameliorate during times of deep mental focus.

Because of its close relationship to other diagnoses, we will use TS as an illustration of how to apply findings from attention research to the study and treatment of clinical populations. Although some may construe TS as a neurological condition, a strong psychological component has been noted for well over a century (Kushner, 1999), and the past decade has seen a revival of behavioral interventions that exploit top-down control (Wile & Pringsheim, 2013). Furthermore, TS symptoms overlap with other conditions, including Obsessive Compulsive Disorder (OCD) and Attention Deficit Hyperactivity Disorder (ADHD). “Pure” TS is hard to find and usually occurs alongside multiple co-morbidities of attention and emotional regulation (Freeman et al., 2000). Hence,
some researchers have characterized TS as an impulse-control disorder related to ADHD and OCD.

Following the logic of RDoC, models of attention would unite TS with impulse-control disorders on the basis of putatively shared neurobiological substrates, as suggested by studies of individuals who have comorbid TS (Freeman et al., 2000) or experience urges (Blumberg et al., 2003; Bush, 2008; Raz et al., 2009; Shafritz, Collins, & Blumberg, 2006; Sowell et al., 2008). In a large-scale study, Freeman et al. (2000) sampled thousands of individuals with TS from twenty-two countries. ADHD and OCD formed the bulk of TS-comorbid diagnoses, contributing to 60 and 27 percent, respectively, of all TS cases. Impairment of the attention system responsible for emotional and behavioral regulation is likely central to these disorders (Raz & Buhle, 2006; Raz et al., 2009). These results highlight the potential for attention research to elucidate both the neurobiological substrate of psychopathology and the mechanisms underlying the clinical effects of current therapies.

Whereas TS was once thought to result from an oversensitivity to dopamine in the basal ganglia, the neurobiological mechanisms appear to be more complex (Felling & Singer, 2011; Leckman, Bloch, Smith, Larabi, & Hampson, 2010). Therefore, pharmacological dopamine blockers, the standard treatment for TS, have fallen short in successfully ameliorating tics for many patients (Peterson & Cohen, 1998; Phelps, 2008; Pringsheim & Pearce, 2010). These drugs frequently induce intolerable side effects, including sedation, parkinsonism, cognitive dulling, dry mouth, fatigue, dizziness, weight gain, and metabolic syndrome (Swain, Scahill, Lombroso, King, & Leckman, 2007). In light of such challenges with pharmacotherapy, efforts have been redoubled to develop cognitive-behavioral interventions for TS (Piacentini et al., 2010), whereas others have examined TS biology more closely (Leckman et al., 2010).

A shared neural circuitry among TS, ADHD, and OCD is consistent with findings that approximately 90 percent of individuals with TS qualify for multiple diagnoses (Freeman, 2007; Robertson, 2006; Scahill, Bitsko, Visser, & Blumberg, 2009). TS, ADHD, and OCD all involve irregularities in the internal neural circuitry that modulate impulse control and in executive attention (Eddy, Rickards, & Cavanna, 2012; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). TS research has focused on cortico-striatal-thalamo-cortical (CSTC) loops involved in habit formation and information transmission between the basal ganglia and the cortex (Alexander, DeLong, & Strick, 1986; Graybiel & Canales, 2000; Leckman et al., 2010). Decreased volume of the caudate nucleus (part of the basal ganglia) in childhood is a predictor of tic severity in
adulthood (Bloch, Leckman, Zhu, & Peterson, 2005); and frontostriatal loop activation, particularly in subcortical structures, influences tic symptom severity (Peterson et al., 1998). Cognitive neuroscientists have further elucidated these subcortical structures as key nodes in the attentional system that may contribute to ADHD (Casey et al., 1997). Both OCD and TS involve include dysfunction of CSTC loops (Harrison et al., 2009); and novel findings from deep brain stimulation suggest that direct modulation of basal ganglia activity can improve OCD symptoms (Welter et al., 2011). Taken together, the neurobiology of comorbid TS blur the distinction between “compulsion” and “tic” and implicate attention as a central component of the condition.

Cognitive-behavioral therapies, which train attention, have been found to surpass pharmacological treatments as effective therapies for TS (Piacentini et al., 2010; Steeves et al., 2012). In response to the considerable empirical evidence supporting habit reversal training (Feldman, Storch, & Murphy, 2011) and comprehensive behavioral intervention for tics (CBIT; Piacentini et al., 2010), recent Canadian guidelines for evidence-based treatment of TS identify cognitive-behavioral approaches as first line treatments for TS (Steeves et al., 2012). These therapies employ classic tools of attention training (AT; Rabipour & Raz, 2012) in that they require sustained attention, awareness, and focus.

Attention may play a key role in tic disorders. When tested with the Stroop task, for instance, groups with TS demonstrate poorer inhibitory function compared to control groups (Eddy et al., 2012; Raz et al., 2009). In addition, tic suppression reduces cognitive performance (Conelea & Woods, 2008), and stress induction raises tic frequency (Conelea, Woods, & Brandt, 2011). We have found preliminary evidence that attention training is effective at reducing tic expression, and six-month follow up data suggest long-term efficacy and increased quality of life (Rabipour & Raz, 2012).

Additional research avenues remain to be explored. For example, using combinations of attention training and neuroimaging techniques, it may be possible to probe the relationships between executive attention training, the unusual ACC patterns in OCD (Freeman et al., 2000), and the abnormal ACC anatomy in adults with TS (Müller-Vahl et al., 2009). Moreover, TS is a unique context for studying impulse control because the overt behavioral expression of tics lends itself to quantitative measurement, even during novel experimental paradigms.

There is evidence that hypnotic suggestion can override processes previously believed to be impermeable to top-down influences (Lifshitz et al., 2013; Raz, Kirsch, Pollard, & Nitkin-Kaner, 2006; Raz, Moreno-Íniguez, Martin, & Zhu, 2007; Raz, Shapiro, Fan, & Posner, 2002);
and hypnosis has been shown to modulate tic expression (Kushner, 1999; Raz, Keller, Norman, & Senechal, 2007). Interestingly, like suggestibility, tic severity peaks during childhood development (Leckman et al., 1998). Because of its ability to bridge controlled and seemingly automatic processes, hypnosis may be an effective tool for attention and TS research alike (Raz, Moreno-Íniguez, et al., 2007). For example, hypnosis can be used to empower individuals to exert executive control over an otherwise involuntary tic. Hypnosis can alter the voluntariness of the semivoluntary tics characteristic of TS in ways that may be similar to attention training, CBIT, or habit reversal training (HRT; Feldman et al., 2011). With regard to HRT and CBIT, hypnosis may have potential as a useful adjunct to attention training. In these training programs, individuals with TS engage in behaviors called “competing responses” when they feel the urge to tic. These competing responses are incompatible with the motions and vocalizations of the tic. Because it can help make voluntary behaviors more automatic, hypnosis may simultaneously increase the elements of suggestion in CBIT and HRT and decrease the difficulty of employing competing responses. Furthermore, hypnosis has proven itself a powerful analgesic (Montgomery, DuHamel, & Redd, 2000), and may provide new ways of reducing the sensory discomfort associated with the premonitory urges that individuals with TS often suffer.

Another approach to clinical intervention has proposed using meditation to improve attention, self-regulation, and emotional control (Perlman, Salomons, Davidson, & Lutz, 2010; Tang et al., 2007; Zeidan, Johnson, Diamond, David, & Goolkasian, 2010). Studies have reported that expert meditators show significant alterations in ACC activity and effortless control over previously challenging and effortful modes of attention (Tang, Rothbart, & Posner, 2012). Such approaches have yet to be applied to conditions such as TS, but there is enough evidence to encourage further investigation.

As research on neural functioning in psychiatric disorders moves from biological reductionism to an integration of neurobiology and psychology, with social science clarifying the contexts of functioning and adaptation, the clinical importance of attention as a mediator of tics and other impulse-related problems suggests the utility of transdiagnostic research frameworks, such as RDoC. The history of approaches to TS shows how the psychiatric pendulum has swung from completely psychological to extremely biological explanations, and then, most recently, back to a more balanced perspective, in which neurobiology, psychology, and social interactional processes all contribute to symptom production. This interactional perspective supports the search for
cognitive-behavioral interventions (Kirmayer & Crafa, 2014; Raz, Keller, et al., 2007).

Although TS represents a particularly interesting condition for the study of attention, it is but one example of how findings on attention systems might be applied to psychiatry. Similar approaches may be useful to help ADHD patients build sustained attention and to help OCD patients alleviate compulsions.

Conclusion

In this chapter, we have emphasized the importance of development in the study of attention as a functional system. Studies conducted over the last decade have revealed key aspects of the neurodevelopment of attention networks. This research shapes our efforts to understand how experience and genetics interact to produce the executive attention network, with possible consequences for developmental problems of children and adults (Posner, 2012a; Posner & Rothbart, 2005).

Approaching attention as a functional organ system – with specific control networks carrying its basic functions – provides a useful direction for psychiatry (Posner & Fan, 2008). Setting aside diagnostic criteria for discrete disorders (as in the DSM), the framework we have presented shows how molecular, neural network, and cognitive studies can be integrated to provide a view of attention that illuminates its role in the development of children and the everyday performance of adults. Disorders of attention comprise an important subset of the problems addressed by modern psychiatry. Attention systems also play a role in adapting to many conditions. Attention training, therefore, can be a powerful tool to influence behavior and modulate cognition, affect, and action in a wide range of problems. As we have shown, linking clinical symptomatology to functional systems through the behavioral and brain sciences breaks down the functional/organic distinction and actually supports the use of psychological and psychosocial interventions for a wide range of putatively “biological” disorders.

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