Attention and learning and memory

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Synopsis:

Following an evaluation of the conceptual overlaps and functional relationships between attentional processes and learning and memory, this article reviews the neuronal macro-systems as well as the role of neurotransmitter-specific projection systems in the mediation of attentional functions and learning and memory. The conceptual relationships and overlaps between the two sets of cognitive functions correspond with overlaps in the neuronal systems involved in the regulation of attentional functions and learning and memory. The relevance of these cognitive and anatomical inter-relationships for the analysis of the cognitive disorders in aging, dementia and schizophrenia is explored in the last section of this article.

Attention and memory

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1. Attention and memory: conceptual issues

Attention describes a set of cognitive processes which act to optimize stimulus detection, discrimination and processing. Attention operates in part by top-down tuning of sensory systems to facilitate the detection of selected stimulus characteristics, such as location and modality; by switching the cortical processing from associational to input modes, and by allocating attentional resources to these operations. Different forms of attention have been categorized, such as sustained, selective, and divided attention. Sustained attention describes the subject's state of readiness to detect rarely and unpredictably occurring changes in the stimulus situation over extended periods of time. Selective attention brings targeted information into the focus of consciousness, while suppressing the detection and processing of non-target signals. Divided attention emphasizes the allocation and the management of limited attentional resources in situations that require attention to multiple stimuli or tasks.

The assumption that attended stimuli are encoded more effectively into memory than less attended ones is straightforward and supported by substantial evidence. However, theoretical frameworks that more fully describe the relationships between attention and learning and memory (L&M) have remained unexpectedly rare. Furthermore, the empirical analyses of interactions between attention and L&M focused on selected aspects of attention and a rather small number of experimental paradigms. For example, increased demands on the division of attention impair stimulus encoding, but generally do not impede the retrieval of previously learned information. Conversely, high demands on memory operations impair attentional capacities, particularly the ability to filter non-target stimuli from being processed. A second major paradigm used in research on the interactions between attention and L&M concerns the impaired learning of extradimensional shifts, as such shifts require the processing of a previously unattended stimulus dimension (e.g., shape, when one had been attending to color).

Attentional processes and capacities represent a cluster of variables contributing to the efficacy of L&M. At the extreme, it is difficult to envision meaningful acquisition of declarative information in the absence of attention. Furthermore, levels of attentional performance vary considerably, and this variation affects the rate of learning and thus the efficacy of memory. Therefore, it is not unexpected that brain mechanisms mediating attentional functions and capacities are also part of the neuronal circuitry mediating L&M.

Functional neuroimaging studies provide strong evidence for the interplay between attention, learning, and memory. Meta-analytic and experimental studies reveal large overlaps between prefrontal and parietal regions activated in attention and memory tasks that are not shared with other (e.g., language processing) domains. Dividing attention at learning leads to reduced activity in prefrontal brain regions associated with subsequent memory, and has long been known to reduce memory performance. Conversely, recent evidence suggests that higher levels of tonic or baseline activity in regions involved in stimulus perception (e.g., parahippocampal regions for perception of scenes) are associated with higher levels of attention to those stimuli, and with better subsequent memory than those preceded by lower tonic activity. Memory also serves to guide attention: Memory-guided visual search activates similar brain regions as does cue-guided visual search, and may even provide greater performance benefits than a visual cue.

In summary, attention, learning, and memory are highly integrated, dynamically interactive processes. This interactivity is reflected both in heavy overlap between the brain systems involved in attention and those involved in learning and memory, and in the mutual influences of attention on memory processing. The following sections describe the neurobiological mechanisms of attention-memory interactions in more detail.

2. Neuronal macro-systems mediating attentional functions and capacities: major research themes

Both lesion studies and functional neuroimaging provide evidence for a distributed cortical network of prefrontal and posterior parietal regions involved in attention. The specific regions involve vary according to the nature of the attentional task. Demands on sustained attention, irrespective of the modality of targets, activate frontal and parietal regions primarily in the right hemisphere. Selective attention and demands for non-target filtering recruit cingulate and other prefrontal regions, again primarily in the right hemisphere. Bilateral fronto-parietal regions typically are activated by tasks requiring the division of attention between multiple targets.

Ongoing research, particularly experiments employing functional magnetic resonance imaging (fMRI), continues to refine the attribution of aspects of attentional performance to specific cortical networks. Results from this research confirm the conceptualization of anterior and posterior attention systems. Posner and Peterson proposed that the anterior attention system, consisting mainly of cingulate and other prefrontal regions, mediates target detection, or the processes involved in the subject’s consciousness of a signal’s presence through producing a response documenting its detection. The posterior attention system involves the posterior parietal cortex and collicular and thalamic regions and controls management of the visual-attentional space.

Essential insights into the neuronal mechanism mediating attentional processes have been gained from research focusing on bottom-up versus top-down selection of stimuli. Bottom-up selection is a function of the intrinsic properties of the stimulus; stimuli compete and cooperate for detection and processing depending on their salience. Bottom-up, stimulus-driven attention is associated with increases in activity in sensory and sensory-associational regions representing the actual stimuli and their location. In addition, increased activity in fronto-parietal networks indicates that stimulus-driven attentional control may also influence the executive management of attentional priorities and resources. In contrast, top-down selection is a function of experience, expectations or instructions. It involves the tuning of receptive field properties, (sustained) anticipatory activity, and suppression of activity in irrelevant regions or modalities, all in order to optimize the detection and processing of expected targets. Top-down attentional control is generally thought to be executed by prefrontal modulation of parietal networks.

The actual mechanisms allowing prefrontal regions to initiate top-down effects, and the cognitive mechanisms and neuronal circuits mediating such top-down effects have remained largely unclear. Likewise, the neuronal circuitries mediating the bottom-up enhancement of stimulus processing, usually in a highly topographic fashion, are not known. As will be discussed further below, evidence on the role of neurotransmitter-specific cortical input systems provide the basis for hypotheses about the neuronal mechanisms modulating the detection of stimuli as a function of top-down, voluntary attention versus the bottom-up influences based on stimulus properties (see also Figure 1).

Evidence from recent fMRI experiments questioned the widely held view that the suppression of irrelevant information or modalities represents an important aspect of prefrontally-controlled top-down regulation of attentional mechanisms. These studies demonstrated that prefrontal mechanisms act to amplify detection of task-relevant information and did not find consistent evidence for top-down suppression of irrelevant stimuli. However, other investigators have found evidence that instructions to ignore one stimulus set in order to more successfully memorize another caused brain activity associated with the ignored stimulus set to be suppressed below a perceptual baseline. As will be further discussed below, the view that selective detection is primarily mediated via enhancement of target stimuli, with little contribution of suppression of non-targets, corresponds with the attentional functions of the cortical cholinergic input system.

Intuitively, motivation is an important factor for engaging top-down mechanisms in order to combat fatigue- or distractor-related decline in attentional performance, to stabilize impaired performance, or to recover from performance impairments. The effects of motivational processes on top-down attention and the neuronal mechanisms via which motivation accesses the anterior attention system to facilitate top-down effects in challenging situations are emerging as an important theme. Increasing the incentives for attentional performance is associated with enhanced activity in fronto-parietal attentional networks, and with activation in additional limbic regions involved in processing errors and response outcomes. Hypotheses concerning the interactions between motivational and attentional processes focus on the regulation of frontal-parietal attention systems via interactions with ventral striatal circuitry known to processes reward, reward expectation, and prediction errors.

While motivation is an a critical factor for top-down attention, stimuli associated with affective information exhibit superior potency for the bottom-up capture of attentional resources. For example, people in a crowded bar manage to ignore the TV until an emotionally-charged symbol or action shifts their attention effectively from ongoing activities to the screen. The neuronal mechanisms allowing such stimuli to consume attentional resources and then drive the subsequent engagement of top-down mechanisms are not well known. However, it is safe to hypothesize, as illustrated in Figure 1, that such stimuli access the brain's main attention systems via reciprocal connections with prefrontal regions (not shown) and with ascending neuronal systems crucially involved in the mediation of attentional functions.

3. Neurotransmitter-specific projections systems in attention and learning.

Substantial evidence supports the hypothesis that the cortical cholinergic input system contributes essentially to the mediation of attentional performance. Cholinergic inputs contribute to both top-down and bottom-up modulation of detection processes, and represent a link between motivational systems and cortical attention systems. Originating from basal forebrain regions, cholinergic neurons receive main inputs from midbrain and telencephalic regions, including the prefrontal cortex, and innervates all cortical areas and layers.

Removal of cholinergic inputs results in persistent impairments in sustained, selective and divided attentional abilities. Furthermore, attentional tasks selectively increase the release of acetylcholine (ACh) from cortical terminals. Evidence suggests that the right hemispheric cortical cholinergic input system is dominant for sustained attention performance; this finding corresponds with evidence from human fMRI studies and from patients with lateralized cortical damage (above).

Recent data indicate that in the prefrontal cortex, a transient cholinergic signal is elicited specifically by successfully detected targets, but not by targets that were missed. The temporal characteristics of these cholinergic signals confirm that essential aspects of the detection process are mediated via increases in cholinergic neurotransmission in the prefrontal cortex. These aspects include disengagement from non-contingent ongoing behaviors or from internal, associational processing, as well as the initiation of target-associated behavioral responses. These findings correspond with Posner's original hypothesis that the anterior attention system mediates the detection of attention-demanding targets (above).

The cortical cholinergic input system is involved both in the activation of the top-down attention system itself, and in the implementation of its downstream effects. Cholinergic inputs to prefrontal regions, including cingulate cortex, specifically contribute to the activation of the anterior attention system, thereby enhancing target detection and activating top-down mechanisms. From there, cholinergic inputs to more posterior cortical regions, including parietal cortex, serve as a branch of the prefrontal efferent circuitry that implements top-down influences on input processing in sensory and sensory-associational regions.

The idea that cholinergic function can be separated into top-down and bottom-up components is supported by the dissociable interactions of these components with other brain systems. For example, ventral striatal modulation of cortical cholinergic activity is limited to the prefrontal cortex. As described above, ventral-striatal modulation, particularly by the nucleus accumbens, is considered critical in situations characterized by the motivated, top-down increase in attentional effort. The modulation of cholinergic inputs to prefrontal regions corresponds with the role of those prefrontal cholinergic inputs in activating top-down effects.

In contrast, bottom-up, stimulus-driven recruitment of the cortical cholinergic input system is believed to involve recruitment of the entire cholinergic projection system, thereby directly influencing sensory processes while also allowing the stimulus to influence the executive management of attentional priorities. Such broad recruitment of the basal forebrain cholinergic system by salient stimuli is mediated in part by ascending noradrenergic projections targeting the cholinergic neurons in the basal forebrain. Noradrenergic neurons in the brain stem are wired to receive information about visceral correlates of salient stimuli and thus “import” information about salience to forebrain regions. Support for the hypothesis that noradrenergic-cholinergic interactions are involved in bottom-up capturing of attentional resources by salient stimuli was generated by experiments demonstrating, for example, that the cortical processing of salient stimuli is attenuated by loss of cholinergic inputs to the cortex or blockade of receptors for noradrenaline in the basal forebrain.

However, the ascending noradrenergic system may exert additional and more specific contributions to attentional performance. There are direct prefrontal projections to noradrenergic neurons in the brain stem, and noradrenergic neurons of the locus coeruleus are activated by attended stimuli. Both of these findings indicate that this ascending system is involved in attentional functions which parallel, at least in part, the attentional functions attributed to the cortical cholinergic input system. The overlaps, interactions, and dissociations between the attentional functions of BF cholinergic and brain stem noradrenergic systems represent an important research topic.

Likewise, the interactions between ascending dopaminergic and cholinergic and noradrenergic systems likely are essential mechanisms in the mediation of attentional processing. The processing of stimuli capable of predicting reward, including the processing of prediction errors, involves mesolimbic dopaminergic systems. Reward and error signals are capable of capturing significant attentional resources, particularly in response to prediction errors. Thus, interactions between dopaminergic systems and the two other ascending modulatory systems may be necessary to optimize arousal and attentional processing. The dopaminergic recruitment of basal forebrain cholinergic neurons is based on tegmental projections to the basal forebrain, and indirectly via dopaminergic projections to the prefrontal cortex and nucleus accumbens and the innervation of the basal forebrain by these regions (see Figure 1). The dopaminergic regulation of the cortical cholinergic input system support the integration of motivation- and attention-related processing. The prefrontal regulation of brain stem noradrenergic neurons and noradrenergic-cholinergic links represent a second major branch of the neuronal systems which, in concert, regulate attentional processes and resources (see Figure 1).

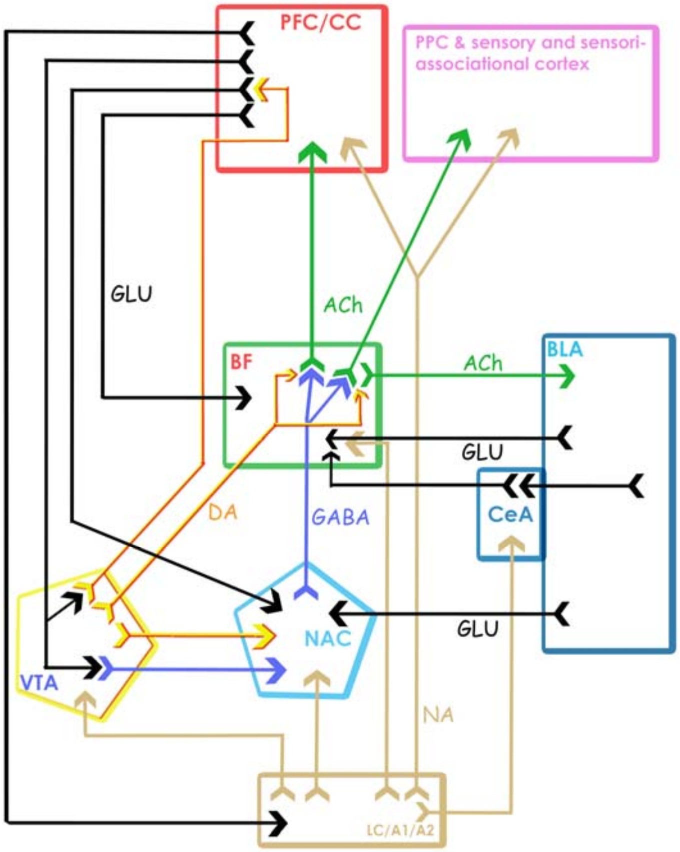

Figure 1. Schematic illustration of the main components of a neuronal network mediating attentional performance and the motivated activation of the cortical cholinergic input system in order to counteract the effects of challenges on attentional performance. The illustration depicts and emphasizes certain direct neuronal projections on the basis of anatomical evidence and importance in the present context. As discussed in the text, neurons using acetylcholine (ACh) as transmitter originate from basal forebrain (BF) regions and innervate all cortical regions, including the prefrontal cortex (PFC), cingulate cortex (CC) and somatosensory and posterior associational regions, including the posterior parietal cortex (PPC). Increases in cortical cholinergic activity contribute to the recruitment of anterior and posterior attention systems, and the cholinergic amplification of input processing in sensory and sensori-associational regions. Cholinergic modulation of the PFC and CC is also involved in the implementation of top-down mechanisms, and the cholinergic inputs to posterior cortical regions are a component of the prefrontal efferent circuitry mediating such top down effects. Increases in top-down effects that are a result of challenges on attentional performance, as well as the subjects' motivation to stabilize residual performance or regain normal levels, depend in part on the regulation of BF neurons by direct projections from the dopaminergic (DA) ventral tegmental region (VTA) and indirectly, via the nucleus accumbens (NAC) and its GABAergic (GABA; γ-aminobutyric acid) projections to BF cholinergic neurons. These midbrain and ventral striatal circuits mediate incentive information and, via feedback from the CC and PFC, information about errors and unpredicted reward contingencies. Therefore, the cholinergic modulation by outputs from these regions form the basis for the integration between motivational and attentional processes. Corresponding with this hypothesis is evidence indicating that control over cortical cholinergic activity by ventral striatal regions is confined to prefrontal regions. In addition to signals predicting reward or reward loss, stimuli associated with salient affective qualities exhibit potent attention-capturing qualities. The cholinergic and glutamatergic (GLU) reciprocal connections between the basolateral amygdala (BLA), as well as additional projections from the amygdala to the BF via the central amygdaloid nucleus (CeA), are thought to be involved in the mediation of such processes. Finally, ascending noradrenergic (NA) projections originating from the locus coeruleus (LC) and the catecholaminergic cell groups in the medulla (A1/A2) innervate major components of this circuits and also receive afferent feedback from the PFC. Thus, ascending noradrenergic projections are hypothesized to contribute to specific aspects of attentional processing in parallel with those attributed to the BF cholinergic system.

4. Ascending modulatory systems mediating attention: involvement in learning

Failure to attend and thus to detect a stimulus involves a failure to produce a representation of this stimulus for encoding. Thus, it is not unexpected that the available evidence on brain regions involved in attention matches, at least partly, the prefrontal-parietal neuronal systems critical for L&M. Indeed, given the critical role of attention for effective encoding, efforts designed to dissociate brain regions involved in attention versus learning pose conceptual challenges. It appears that a system of cortical regions processes stimuli at levels giving rise to awareness about these stimuli, however, the source of such processing of stimuli, whether it is a result of attentional or mnemonic operations, is not indexed in these regions.

The overlapping roles of ascending modulatory systems in attention and L&M are less well documented. In fact, several animal studies on the effects of loss of cortical cholinergic inputs have suggested that L&M do not depend on the integrity of these neurons, and that therefore the neuronal circuitries mediating attention and learning and memory could be dissociated. However, the lack of effects of, for example, lesions of the basal forebrain cholinergic system on L&M in animals may reflect, at least in part, the limited degree to which conventional animal tasks for L&M assess attention-requiring encoding and retrieval of declarative information. By contrast, more recent studies using tasks that require involving attention to stimuli or attention shifts find that learning is readily impaired by manipulations of levels of cortical cholinergic neurotransmission. Recent studies in humans have begun to simultaneously measure the cognitive and hemodynamic effects of drugs modulating cholinergic neurotransmission (“pharmaco-fMRI”). These studies indicated that drug-induced increases in cholinergic transmission enhance attentional mechanisms and the selectivity of stimulus processing during encoding. These results confirm the overlapping role of the cholinergic system in attention and learning, at least in situations requiring the encoding of attended stimuli. Similar conclusions have been drawn based on data from experiments in animals and humans on the role of the noradrenergic system in attention and learning.

5. Attention and learning: relevance for aging and neurodegenerative and neuropsychiatric disorders

Normal and pathological aging, including mild cognitive impairments and the dementias are characterized by coinciding impairments in attentional functions and learning.

In non-demented aging, reduced attentional function is typically thought to be the major source of age differences in forgetting. There is some debate as to the nature of age deficits in attention function, with some theories emphasizing age differences in the *amount* of attentional resources, whereas others emphasize age differences in the *allocation* of attention, particularly deficits in inhibition. Across these perspectives, there is broad agreement that the controlled, top-down aspects of attention are those that show the greatest declines, whereas more automatic, bottom-up influences are relatively spared. Decreases in top-down attention are often ascribed to atrophy and reduced function in prefrontal cortex and basal ganglia structures, the structures that typically show the largest volume reductions in both longitudinal and cross-sectional studies of normal aging. These changes are thought to be largely responsible for age differences in most areas of cognition, although recent longitudinal evidence suggests that changes in select medial temporal lobe structures may be greater than suggested by earlier cross-sectional studies. Moreover, age-related attentional impairments may be a result of dysregulation and eventual degeneration of basal forebrain cholinergic projections to cortical regions.

The idea that the reduced availability of attentional resources is a major contributor to age differences in learning and memory receives substantial support from studies showing that asking young adults to divide their attention between multiple tasks (thus reducing the attentional resources available to any single task) often leads to results similar to those of older adults under single-task conditions. This is especially the case when the performance measure is subsequent memory for material studied under divided attention. Like older adults under single-task conditions, young adults studying under divided attention conditions show less activity in left frontal brain areas associated with later successful memory than do young adults studying under single-task conditions. On behavioral tests, the memory costs of divided attention are often similar for young and older adults, but older adults show larger impairments on the secondary task.

On the positive side, reducing the demand for top-down control often improves both memory and brain function for older adults. For example, intentional memory instructions ("memorize the words") require participants to engage top-down control to choose and implement a strategy for processing words that will support their later memory. Older adults typically perform much worse than do young adults under these conditions, and show less activation in left prefrontal cortex areas involved in subsequent memory. By contrast, when given instructions that guide attention to the memory-supporting semantic aspects of a stimulus ("Does the word mean something abstract, or concrete?"), memory is improved, and older adults often show prefrontal activations that are at least as great as those shown by young adults.

While initial findings focused on age-related under-activations of frontal brain regions involved in controlled attention and memory, more recent data shows that in many cases, older adults show more activation, or activate additional brain regions that young adults do not. In many cases, this additional activation is linked to better performance, especially on memory tests. Patterns of under- and over-activation of frontal brain regions by older adults may be related to failures of top-down, "proactive" control, and later "reactive" attempts to compensate.

A recent meta-analytic review suggested that reduced or disrupted activations may be more common in right anterior frontal regions (often thought to be involved in high-level controlled strategic processing), perhaps reflecting a failure to adequately engage top-down processing to organize efficient task execution. By contrast, left frontal regions were more often associated with greater activation by older adults, perhaps reflecting greater engagement of lower-level processes in an attempt to compensate. Further supporting the idea of an age-related shift to reactive control, memory-related frontal brain activations have an extended time course for older adults under conditions with high control demands (remembering words studied once), but equivalent time courses to young adults under conditions with low control demands (remembering words studied 20 times). This shift is specific to frontal regions; parietal brain regions involved in successful recognition do not show a similar sensitivity to control demand.

Whereas attention and dopamine function are the focus of most research on normal aging, deficits in memory and cholinergic function are the characteristic features of Alzheimer's disease. However, Alzheimer's disease is also associated with marked deficits in attention. For example, the ability to divide attention between two ongoing tasks is substantially impaired in AD, even when performance on the individual tasks has been matched with that of healthy controls.

Attention deficits are not easily detected in the earliest stages of the disease, which is primarily marked by memory deficits. However, difficulties with attention precede the breakdowns in language and visuospatial function that occur at the moderate and severe stages of the disease. It is not clear which aspect of attention (selective, divided, or sustained) is the first to deteriorate in AD. Several reports indicate that very demanding selective or divided attention tasks show declines early in the disease process, whereas simpler sustained attention tasks only show deficits at later stages or under conditions (e.g., stimulus degradation) that increase difficulty. However, there have also been reports of preserved performance on selective attention tasks in patients with reduced sustained attention performance.

Within a domain, the detection of AD-related deficits in attention may depend not only on disease severity but also on the specific processes being tested. In selective attention, patients are often able to shift and engage attention appropriately in response to a valid cue. However, they appear to be impaired at disengaging attention from an inappropriate location following an invalid cue, especially if the task involves discrimination of a target stimulus from nontargets rather than simple detection.

For both normal aging and AD, a heuristic description is that attention performance deficits become more obvious with increased complexity or control demand. Functions that require little or no top-down control generally show little or no deficit. Examples include the engagement of spatial attention by the sudden onset of a peripheral cue, or the inhibition of attention's return to a previously-attended location.

Deficits can be especially large on so-called “executive function” tests, which require top-down control in order to override automatic responses driven by bottom-up stimulus characteristics (e.g., moving one's attention away from a peripheral cue in the antisaccade task, responding to ink color rather than word identity in the Stroop task) or to maintain and rapidly switch between multiple response rules (e.g., dual-task procedures). The memory problems of AD may contribute to poor performance on tasks designed to measure attention, as patients may have difficulty both with remembering the response rule and with its execution.

The specific abnormalities in the regulation of integrity of neuronal systems responsible for the age- or dementia-related impairments in attention and encoding remain not well understood. However, structural and regulatory age differences in basal forebrain cholinergic projection have been extensively documented in brains of humans and animals. Furthermore, as the development and maintenance of forebrain cholinergic neurons depend on nerve growth factor (NGF) signaling via several neurotrophic receptors, expressed selectively by cholinergic neurons. The availability of such receptors in the is dramatically reduced in the brains of subjects with mild cognitive impairments. Given the central role of the cholinergic system in attention (above), these reductions support the hypothesis that the attentional and related cognitive impairments observed in these patients are due, at least to a significant part, to dysregulation of forebrain cholinergic neurons. Subsequent loss of forebrain cholinergic neurons during the onset and progression of dementia contributes essentially to the severity of impairments in attention and memory.

Impairments in both the activation of relevant stimuli and the inhibition or filtering of irrelevant stimuli are among the fundamental cognitive dysfunctions of schizophrenia. These disruption of attentional abilities are reflected in impaired learning and memory. For example, the exhaustion of attentional resources for encoding of relevant stimuli contributes to impaired maintenance and updating of patients' memory, thereby perhaps contributing to the development of aspects of positive symptoms. Abnormal metabolic responses to cognitive challenges have been observed in fronto-parietal networks, although the specific neuronal mechanisms underlying the attentional dysfunctions of schizophrenia are not fully understood. However, available evidence strongly suggests an abnormally reactive dopamine system in schizophrenia. Given the role of dopaminergic-cholinergic interactions in the motivational regulation of attentional performance (above), both cortical cholinergic recruitment of the anterior attention system and the cholinergic mediation of input processing in sensory and sensori-associational regions are expected to be highly abnormal in schizophrenia. Evidence from animal models of this disease corresponds with this hypothesis, as does the demonstration of down-regulated muscarinic receptors in the cortex of schizophrenic patients. It is widely assumed that abnormalities in the development of cortical, particularly prefrontal, circuits represent a primary neuropathological foundation for schizophrenia. These abnormalities may in turn lead to the dysregulation of the ascending, bottom-up modulatory systems (above). Moreover, the dysregulated release of these neuromodulators interacts with defective cortical target circuits, collectively mediating the attentional and encoding dysfunctions characteristic for schizophrenia.

6. See also

Acetylcholine
Aging of the brain
Arousal

Alzheimer’s disease
Basal forebrain
Cingulate cortex
Cognition in aging and age-related disease
Dementia
Dopamine
Locus coeruleus
Noradrenaline
Parietal cortex
Prefrontal cortex
Schizophrenia

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