Attention and its disorders

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This chapter focuses on the clinical aspects of attention including anatomy, cognitive neuropsychology, disorders, and functional imaging evidence for the role of attention in cognition. Particular emphasis is given to selected aspects of visual attention. Imaging studies discussed are primarily functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). In addition, some evidence will be provided from the time-honoured clinical method of lesion studies.

Numerous cognitive processes come into play as one reads this chapter. In fact, it takes little introspection to realize the necessity for visual, language, working memory, and declarative memory (among other) systems in the reading process. Perhaps this chapter will contradict or confirm a cherished scientific belief, thus bringing limbic systems into play. However, the proper operation of all these systems would not be possible without a function that allowed the appropriate selection of stimuli, maintenance of concentration, and interactions with space and time. That cognitive function is attention. Indeed, it could be argued that while most other cognitive systems can operate somewhat independently of one another (e.g. patients with aphasia can still see just as well and patients with pure amnesia can still speak) none of them could function at anywhere near normal levels without the appropriate attentional interactions. Without attention, coherent thought itself would be impossible.

The focus of this chapter will be on the clinical aspects of attention including anatomy, cognitive neuropsychology, disorders, and functional imaging evidence for the role of attention in cognition. However, as the short space allotted to this chapter allows only a brief overview of this domain, the discussion will be focused primarily on selected aspects of visual attention. The interested reader should see the references for additional information. The imaging studies discussed in this chapter primarily fall into the domain of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). In addition, some evidence will be provided from the time-honoured clinical method of lesion studies.
Definition

Attention has been defined in many ways over the years, yet none of the definitions has improved substantially on the one given by William James in 1890. In his book, *The Principles of Psychology*, James stated:

*It [attention] is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state.*

In this one paragraph, James provided both a definition of attention and a remarkably prescient description of one type of attentional deficit, that of a confusional state. As James’s statement implies, and recent research has demonstrated, attention results in the preferential processing of various types of cognitive information. For example, attentional enhancement can be demonstrated for objects in the environment, for actions, for perception of our own internal states, for thoughts, for space and for time. The multidimensional nature of attention has led theorists to wonder whether the concept of attention is well-conceived, *i.e.* whether it refers to a single or clearly definable set of functions. The approach taken in this chapter is that while attention is not a unitary concept, it does represent a cohesive set of processes, which serve to enhance sensory, motor and cognitive processing.

Attentional components

Figure 1 presents a schematic for the basic organization and anatomy of attention. Each of these levels will be discussed in turn. Any discussion of attention must first comment on the relationship between attention and arousal since the terms appear so closely related. It seems logical, for example, that an organism with impaired arousal would also have impaired attention. The reverse, however, is not necessarily true as normally alert individuals can show attentional deficits. Furthermore, states of hyperarousal (*e.g.* pain and fear) may interfere with proper attentional functioning.

The core of the arousal system includes the mesencephalic reticular formation and portions of the thalamus (reticular and intralaminar nuclei). Together, these regions comprise one part of the ascending reticular activating system (ARAS). The other components of this system of a series of brainstem (substantia nigra, ventral tegmental area, raphe nuclei, and locus coeruleus) and basal forebrain nuclei. Activity in the ARAS results in a wakeful state, desynchronizes the electroencephalogram, and modulates...
neuronal responsivity. Changes in the state of arousal will thus clearly influence cortical and subcortical areas involved with attention. The opposite relationship is also true and changes in the attentional state of an organism can influence the activity in the ARAS. For example, Kinomura and colleagues demonstrated the influence of attention on ARAS activity by using PET to compare regional cerebral blood flow (rCBF) when subjects were awake but resting versus when they were engaged in attentionally demanding tasks. During the state of high attention, rCBF increased markedly in the mesencephalic tegmentum and the intralaminar nuclei of the thalamus (among other regions) confirming the hypothesized influence. Figure 2 shows the activations in the thalamus and mesencephalic tegmentum.

In keeping with the multidimensional nature of attention, several different varieties have been identified. This situation is no different than in other cognitive domains. For example, memory processing has been divided into declarative, episodic, implicit, etc subgroups, while in the language domain there are fluent and non-fluent aphasias among other distinctions. The taxonomy of attentional divisions has tended to be confusing, however, as it has often depended on what is being attended to. For example, the term selective attention can refer to the selection of objects, their attributes, or a portion of space.
Selective attention is one of the most studied aspects of attention and is the aspect of attention most often referred to when discussing the brain’s limited processing capacity and the need to select particular targets among multiple stimulus streams. What exactly an organism is selecting will depend on the task being performed. Selection can encompass many domains, and evidence has accumulated for both object and space based attentional selections. Divided attention involves monitoring of several stimuli at once. Vigilance refers to the sustained aspects of attention. Vigilant behaviour can include both sustaining attention to a particular stimulus over time or to the detection of and response to any unpredictable or rare event. Finally, the controlled aspects of attention refer to behaviour in which attention to one activity is stopped so that attention can be directed to another stimulus.

Anatomical and behavioural models

One set of cognitive models has postulated that various aspects of attention act in a top-down manner to bias preferentially the processing of stimuli. As illustrated in Figure 1, top-down refers to the influences of heteromodal (posterior parietal and prefrontal) and limbic cortical areas on unimodal visual, auditory and somatosensory cortices in order to modulate the processing of stimuli based on the cognitive and motivational preferences of the organism. Top-down models of attention have also been conceived as a type of mental spotlight, which enhances...
processing of the illuminated (i.e. selected) item\textsuperscript{13,14}. Two main anatomical models have emerged for this organization of attention. Although the model developed by Mesulam comes from a more anatomical viewpoint, and that of Posner stresses the particular psychological operations involved, both models bear a remarkable similarity in the hypothesized brain regions and cognitive processes (Fig. 3).

Mesulam’s model is characterized by each of the main cortical regions containing a high-level abstract map of the world: a sensory-representational map in the parietal cortex, a motor-exploratory-map in the premotor cortex/frontal eye fields, and a limbic-motivational map in the cingulate cortex and possibly insula. This anatomical organization was based primarily on tract tracing studies in primates and behavioural studies of patients with neglect (see Mesulam\textsuperscript{15,16} for references).

The model proposed by Posner and colleagues focuses on the cognitive operations performed by each of the regions. Thus, the posterior attentional network is responsible for moving the focus of attention. This operation includes disengaging attention from its current target (controlled by the parietal cortex), moving attention to a new target (controlled by the superior colliculus) and engaging attention at the new target (controlled by the pulvinar). The anterior attentional network is involved with detecting salient events and preparing motor responses. Finally, the vigilance network is in charge of sustaining attention and maintaining a state of alertness\textsuperscript{17}.

Both Mesulam’s and Posner’s models were initially intended to explain the spatial aspects of attention and not the interaction of attention with particular object features. In his 1981 article, Mesulam himself noted that his theory did not account for all aspects of attention\textsuperscript{15}. In addition,
only Mesulam’s model comments on how neuronal responses might be affected by attention\textsuperscript{15}.

Despite these shortcomings of these models, both accurately characterise the cortical and subcortical brain regions associated with top-down attentional behaviours. Numerous functional imaging studies have confirmed and re-confirmed the involvement of these top-down areas (posterior parietal, frontal eye field and cingulate/supplementary motor cortices) in various aspects of attention. Tasks producing activations in these regions include sustaining attention\textsuperscript{18}, shifting attention covertly (without eye movements)\textsuperscript{19-22}, shifting attention overtly (with eye movements)\textsuperscript{23,24}, and motivational biasing of attentional behaviour\textsuperscript{25}. Figure 4 illustrates the anatomy of regions putatively involved with the top-down aspects of attention. Note that activation of the temporo-occipital junction (TOJ) is likely to reflect top-down influences on the visual system, rather than being part of the top-down system \textit{per se}.

Recent attentional models have begun to incorporate the concept of bottom-up competition among stimuli (actually their neuronal representations) to explain the effects of various target types on attention, the dynamic interaction between perception and attention, and the fine focus of the attention spotlight\textsuperscript{26}. A ‘biased competition’ model suggests that competition occurs at the level of the sensory association cortices among neurons representing different objects or

\textbf{Fig. 4} Regions activated by covert shifts of spatial attention. Images were acquired using fMRI. Activated regions are significant at $P < 0.05$ corrected for multiple comparisons. The group performing this task ranged in age from 24–80 years demonstrating that these activations are seen consistently across the adult ageing spectrum. Key: INS, insula; IPS, intraparietal sulcus; FEF, frontal eye fields; TOJ, temporo-occipital junction (probably includes region MT+); TPJ, temporo-parietal junction.
locations in the environment. A further modulatory signal is provided by the top-down attentional cortical centres, which provide feedback to the visual regions. Competitive interactions take place across the stimulus environment in a parallel manner. Attention thus emerges as a combination of feed-forward signals from the visual cortices (bottom-up) and feed-back signals from the parieto-frontal-limbic network (top-down). The combined interactions are thought to bias positively neurons representing the attended target(s) to ‘prevail’ in their interactions. Presumably, similar competitive interactions occur in other sensory cortices. In addition, neurons representing unattended stimuli are thought to be suppressed in their responses.

The principles of top-down and bottom-up interactions are demonstrated in Figure 5, which is taken from the article by Kastner and Ungerleider. The figure demonstrates that in the absence of attention, a visual stimulus is still able to activate visual association cortex (Fig. 5A). In the presence of attention, activation is greater at sites such as V4, which are connected with up-stream (top-down) cortical areas (Fig. 5B). When visual stimulation is removed, attention still affects the baseline activity in visual association cortex (Fig. 5C). Thus, it appears that attention can modulate baseline neural activity in order to prepare a specialized region for processing some type of anticipated stimulus. Attention further modulates the response of a region when the appropriate stimulus appears.
The concepts underlying the biased competition model are also important because they illustrate that attentional interactions can take place potentially at all levels of sensory processing. These multilevel attentional concepts have been incorporated into many current theories of attention2,29.

**Disorders of attention**

Given the importance of attention to sensory and cognitive processing, it is not surprising that attentional disorders are among the most common and most devastating neurological conditions. The main attentional disorders are confusional states, partial (domain-specific) attentional syndromes, and hemispatial neglect.

**Confusional states**

A confusional state (or delirium) is a global change in mental status wherein the principal cognitive deficit is a change in the overall attentional tone. It is the most common disturbance of mental status seen by physicians. Associated symptoms can include incoherent thinking, distractibility, perceptual disturbances including illusions or hallucinations, dyscoordination, delusions, impaired judgement, reduced insight and agitation. Some of these disturbances may arise because of the attentional disorder while others may arise separately2.

Patients in a confusional state are usually disoriented and their memory is impaired. They may appear to have mild-to-moderate associated cognitive deficits such as an anoma, dysgraphia, dyscalculia, or constructional difficulties2. The attentional nature of these disturbances may become apparent if the patient is given additional assistance in a task. For example, extra-encoding trials on memory tests may allow the patient with a mild confusional state to overcome partially the apparent amnestic disturbance.

Despite wide-spread cognitive disturbances, patients usually have no lateralizing neurological signs and primary motor and sensory functions are generally intact. When neurological signs occur, they may include a coarse tremor, myoclonus or asterixis as an indicator of the patient's underlying metabolic disarray2. Focal neurological signs may be seen, however, when the confusional state arises because of intrinsic central nervous system disease (e.g. stroke).

The main causes of confusional states can be divided into six major classes, which are listed in Table 1. Referring back to Figure 1, a confusional state can involve any of the levels of the attention-arousal
system. The actual mechanisms of attentional disruptions include multifocal disorders, strategic focal lesions, or interference with neurotransmitter functions (particularly cholinergic). As listed in Table 1, the focal anatomical regions associated with a confusional state include the parahippocampal-fusiform-lingual gyri in either cerebral hemisphere, and right-sided lesions of the posterior parietal and inferior prefrontal cortex.

<table>
<thead>
<tr>
<th>Diagnostic class</th>
<th>Examples and additional information</th>
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<tbody>
<tr>
<td>Toxic-metabolic encephalopathy</td>
<td>Renal insufficiency, hepatic failure, sepsis, endocrine disorders, severe anaemia, electrolyte and water-balance disorders, drug withdrawal or intoxication</td>
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<tr>
<td>Environmental stressors</td>
<td>Circadian rhythm disturbances (e.g. in the intensive care unit), immobilization, and sensory deprivation (e.g. sudden changes in vision or hearing)</td>
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<tr>
<td>Multifocal brain lesions</td>
<td>Meningitis, encephalitis, closed head injury, multiple strokes (e.g. shower of emboli), and subarachnoid haemorrhage</td>
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<tr>
<td>Epilepsy</td>
<td>Confusional states can be seen after a generalized seizure or in the case of non-convulsive status epilepticus</td>
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<tr>
<td>Space occupying lesions</td>
<td>Subdural haematoma</td>
</tr>
<tr>
<td>Focal brain lesions</td>
<td>Lesions of the parahippocampal-fusiform-lingual gyri in either cerebral hemisphere, or right-sided lesions of the posterior parietal and inferior prefrontal cortex</td>
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There have been few functional imaging studies of patients in a confusional state, probably because of the difficulties examining such patients. In a study of 50 patients undergoing cardiac surgery, six were found to have a delirium based on clinical examination. These six and another three patients, whose clinical diagnosis was not clear, were found to have perfusion abnormalities by $[^{99m}Tc]$-HMPAO single photon emission computed tomography (SPECT). Abnormalities were noted in the left temporoparietal region (5 of 9 patients), right temporoparietal region (4 of 9), frontal cortex on the left (1 of 9) or right (3 of 9), and the right occipital cortex (2 of 9). Five of nine patients had two or more areas of involvement. In a single patient study, a SPECT scan demonstrated right parieto-occipital hypoperfusion in a delirious patient. These functional imaging studies are consistent with the concept of a network of brain regions contributing to attention. Damage to any part of this network may produce a confusional state.
although some regions (e.g. temporoparietal cortex) appear to be more critical than others.

**Partial attentional syndromes**

Attentional impairments can also present more focally as domain-specific or ‘partial’ attentional syndromes. These syndromes are not well defined because partial attentional impairments tend not to present as separately definable syndromes, rather they are manifest as reduced performance in one or more cognitive domains. For example, changes in visual-based attention could result in reduced detection of stimuli in the environment, while changes in language-based attention could present as reduced verbal fluency. In both these examples, the clinician must be alert to the possibility of an attentional disruption rather than a visual disorder or an aphasia, respectively.

Domain specific attention deficits have been produced in normal individuals using tasks based on the concept of inattentional stimulus processing. Such tasks present subjects with stimuli, which they either attend or ignore. By examining the difference between the attend and ignore conditions, the effects of attention on domain specific processing can be observed. Rees and colleagues, for example, examined domain-specific attentional effects on letter string and picture processing31. They found that attention was able to influence, differentially, processing within the visual system for words (left occipital activation) versus pictures (bilateral occipitotemporal activations) even when the words and pictures were both presented simultaneously at fixation. Attention to words also enhanced activations throughout the language system31.

**Hemispatial neglect**

The last attentional disorder to be discussed is hemispatial neglect. This disorder, one of the most clinically dramatic in neurology, is characterized by the inability of the patient to orient towards, respond to, or report on, stimuli on the contralesional side of space32. Neglect is a multimodal deficit and may affect any or all sensory modalities, motor behaviours or even the internal representations of memories and other thoughts. Most often, the left hemispace is neglected, as the disorder is more frequent and severe following right hemisphere injury.

Clinically, the patient’s head and eyes may be directed entirely towards the ipsilesional space (usually right). When there is an accompanying motor deficit, the patient may deny any problem with the affected limb (anosognosia), may say they are moving the limb normally as it hangs
limply at their side, or may fail to recognize the affected limb as their own. Patients with neglect may fail to groom themselves properly on the neglected side, or may fail to eat food on the neglected side of the dinner plate. When reading, the patient may start towards the middle of a line rather than on the left, for example, reading ‘your eyes’ when shown the phrase ‘close your eyes’. It is important to note that basic sensory or motor disorders are not part of the neglect syndrome, although they may be present.

The phenomenon of extinction may occur either together or separately from neglect. Extinction is diagnosed by the patient being able to detect stimuli presented separately to either side of space, but only detecting one of the stimuli (usually right) when they are presented simultaneously. At times, the deficits associated with neglect are less dramatic and may only be apparent when the patient is asked to perform more specific tests such as bisecting lines or searching for targets among a set of irrelevant stimuli.

Numerous theories have been proposed to account for the deficits in neglect. Unfortunately, space constrains any discussion other than just a listing of various theories and their chief proponents. Explanations have included a distortion of internal representations (Bisiach), release of asymmetrically opposed attentional vectors (Kinsbourne), impaired attention towards the affected hemispace (Heilman and colleagues), impaired motor intentional behaviour (Heilman), impaired disengagement of the attentional focus from ipsilesional stimuli (Posner), distortion of the spatial reference frame (Jeannerod, Karnath), multidimensional impairment of selective attention (Mesulam), and altered premotor planning behaviours (Rizzolatti).32,33

Lesion sites causing neglect have been found throughout the network of cortical and subcortical areas responsible for attention. These regions include the posterior parietal cortex/temporoparietal junction, frontal eye fields, cingulate and supplementary motor cortex, basal ganglia, thalamus, midbrain and superior colliculus. Typically, the lesions are on the right.

Only a few recent studies have been able to examine directly the deficits of neglect and extinction with functional imaging technology. Vuilleumier and colleagues studied a patient with neglect due to a right parietal lesion, who had intact visual fields. Event-related fMRI was
used to show that non-perceived stimuli still activated the visual cortex. When stimuli were occasionally perceived, the visual cortex activations were expanded and activations were also seen in the left parietal cortex. Measures of inter-regional correlations involving frontal, parietal and visual areas also increased when the subject was aware of a stimulus. This study confirmed both bottom-up and top-down aspects of attentional processing, and was consistent with the theory that attention may be critical for conscious awareness\textsuperscript{31,34}.

**Conclusions**

Numerous recent imaging studies have begun to reveal the multifaceted nature of attentional behaviour and its disturbances. More importantly, long-held theories regarding attentional contributions to perceptual processing, motor selection and the internal choice of particular thoughts can now be studied directly. Event-related fMRI, event-related potential studies and newer studies with magneto-encephalography will allow improved spatial and temporal localization of the processes underlying this important aspect of cognition.

**Key points for clinical practice**

- Attentional disturbances are ubiquitous in clinical practice. However, the multimodal and protean nature of the disturbances may make them difficult to recognize.
- A confusional state is arguably the most important attentional disorder to diagnose, as its presence usually indicates an underlying acute medical condition.
- Domain-specific attentional changes must be specifically sought, through careful cognitive testing. Identifying this class of disturbances is important when trying to distinguish disorders within a modality *versus* a partial deficit of attention. For example, in examining patients with memory complaints, it is critical to demonstrate whether the patient has a true amnestic disturbance *versus* a disorder of attention, as the anatomy and treatment of the associated disorders may be very different.
- Hemispatial neglect should be sought particularly in patients with right hemisphere lesions. Because of the nature of neglect, *i.e.* a lack of awareness for the neglected hemispace, patients will never directly complain of this deficit although it is frequently noted by care-givers.
Acknowledgement

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