

INTENTIONAL NEGLECT

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1. ABSTRACT

The neglect syndrome has been defined as a failure to report, respond or orient to novel or meaningful stimuli presented to the side opposite of a brain lesion when this failure can not be attributed to elemental sensory (e.g., hemianopia) or motor (hemiplegia) deficits. This failure to report, respond or orient can be induced by attentional, representation-memory, and intentional deficits. The four major intentional deficits that can be associated with neglect include, akinesia (body part, directional and hemispatial), impersistence, defective response inhibition and motor perseveration. In this article we define and discuss each of these intentional disorders, describe how to test patients for these disorders and the neuropsychological and pathophysiological mechanisms that might be associated with these disorders.

2. INTRODUCTION

Welch and Stuteville (1) demonstrated that unilateral ablation of the monkey's dorsolateral frontal lobe cortex, in the region of the arcuate gyrus, induced a disorder similar to the unilateral or hemispatial neglect observed in humans with parietal lesions. After unilateral ablation of the arcuate gyrus (e.g., right), the animals failed to respond to stimuli presented on the opposite side (contralesionally). Because these animals did not appear to be weak, their failure to respond was attributed to unawareness or inattention to these contralesional (e.g., left sided) stimuli. Watson, Miller and Heilman (2), however, were familiar with patients who had Parkinson's disease: even in the absence of weakness, inattention or unawareness, these subjects often failed to initiate movements, a condition called akinesia. Parkinson's

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disease is a disorder of the basal ganglia, and the basal ganglia has many connections with the medial and dorsolateral frontal lobes. In addition, many areas of the dorsolateral frontal lobes also have connections with the motor cortex, at the caudal end of the frontal lobes. Based on these connections, Watson, Miller and Heilman (2) suggested that the neglect associated with dorsolateral frontal lesions might be associated with an akinesia rather than sensory neglect. To test this hypothesis, they trained monkeys in a crossed response test: when stimulated on the right hand, the animals were to move their left arms to a target in left space, and when stimulated on the left hand, they were to move their right arms to a target in right space. After unilateral (e.g. right) dorsolateral frontal cortical ablations, monkeys stimulated on the contralesional (left) hand might fail to respond with their right hand. In this case, inattention would be considered to be the basis of the animals' neglect. However, if the right dorsolateral frontal cortical ablation did not induce hemiparesis, and these monkeys responded with the right hand to left sided stimulation but failed to move the contralesional (left) arm to ipsilateral (e.g., right) stimuli, they would be considered to have a type of akinesia or an action-intentional deficit. After unilateral dorsolateral frontal ablations, Watson Miller and Heilman (2) found that monkeys' response failure was consistent with akinesia rather than inattention. We will call this deficit intentional neglect.

The brain has a limited capacity to fully process stimuli. Organisms with limited capacity system have to decide, which stimuli to fully process and which stimuli not to process. In general, organisms elect to process stimuli that are of importance and ignore stimuli that are irrelevant. The importance of a stimulus is often determined by the organism's biological needs (drives) and long term goals. Because the meaning of novel stimuli have not been determined, organisms will at least temporarily attend to most novel stimuli. The process by which stimuli are triaged is called attention, and inattention is the failure to fully process important stimuli.

The brain not only has a limited ability to process multiple stimuli, but also has a limited capacity to plan and initiate actions. Thus, the brain must select acts which are important for long term goals and biological needs. There is also a triage system that helps the organism decide when to act or when to not act, when to persist at an action and when to finish an action. We will call this motor triage process "intention." The functions of the intentional system in many respects parallel those of the attention system, hence intentional deficits often have parallels to attentional deficits. Thus, unawareness or inattention is parallel to akinesia, distractibility to defective response inhibition, defective vigilance would be similar to impersistence, and a failure to habituate or extinguish stimuli would be similar to motor perseveration. In patients with intentional neglect we can see many of these deficits which are often asymmetric, being more severe in one part of space or in one part of the body (contralesional) than on the other side (ipsilesional).

In this article, we will first describe each of these

intentional disorders in more detail, including subtypes of each category. We will also discuss how to examine patients for these disorders. In subsequent sections, we will discuss the pathophysiological and neuropsychological mechanisms that may be associated with these disorders. The networks that mediate the intentional systems are widely distributed, but the right hemisphere's frontal lobe plays a critical role. Hence, our discussion will focus on the special role the frontal lobes and the right hemisphere appear to play in the computation of these intentional decisions.

3. AKINESIA

3.1. Definition

Akinesia is the failure to initiate a movement when a movement is required. Although there are many causes for a failure to initiate movement, disorders of comprehension, attention, or perception that lead to a failure of movement should not be termed "akinesia". In addition, disorders of the motor system, including the motor unit (lower motor neuron, myoneural junction, and muscle) and the upper motor neuron (pyramidal or corticospinal system) may be associated with an initiation failures, but akinesia is defined by an initiation failure that cannot be attributed to dysfunction in these motor systems. Akinesia is caused by a failure to activate these motor neurons.

3.2. Testing

The clinician can use three major methods to distinguish an akinesia from dysfunction of the motor systems. One is behavioral, a second physiological and the third depends on structural imaging to find the locus of a lesion. With regard to behavioral tests, certain types of akinesia are present under certain sets of circumstances and absent in others. Hence, if the clinician can demonstrate that a patient makes a movement in one set of circumstances but not in another, then the clinician cannot attribute failure of movement to elemental motor dysfunction. For example, after a right hemisphere lesion a patient might fail to spontaneously move their contralesional (e.g., left arm) but (as will be discussed below) if the examiner moves the patient's arm from contralesional (left) hemibody space to the ipsilesional (right) body space the patient may then be able to show good movement of this arm. If, however, the clinician cannot show that a certain body movement occurs under any circumstances, to demonstrate that the brain lesion does not involve the elementary motor system the clinician might have to depend upon brain imaging (e.g., CT or MRI) or pathology. Electrophysiological methods such as motor evoked potentials induced by transcranial magnetic stimulation can also assess the integrity of the corticospinal system as well as the motor roots and nerves. For example, Triggs *et al.* (3) reported a patient with a limb akinesia who on structural imaging did not show involvement of the motor system. Transcranial magnetic stimulation supported this radiological impression, revealing comparable thresholds for electromyographic activation of the muscles of both arms, and normal central motor conduction times.

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As we discussed above, attentional deficits might masquerade as a form of akinesia. In many patients, the two might even co-exist. To dissociate inattention from some forms of akinesia as described above, one has to dissociate input from output. These methods will be discussed below when we describe the subtypes of akinesia.

3.3. Types of Akinesia

There are several forms of akinesia, but we have divided them into three major categories: 1. body part; 2. action space; 3. stimulus-response conditions. These categories are not mutually exclusive and even might be interactive.

3.3.1. Body Part

Akinesia may involve the eyes, the head, a limb, or the whole body.

3.3.1.1. Limb Akinesia

An akinesia of the limb might, as we will discuss below, be dependent upon where the action takes place. However, in the clinic, one encounters patients who, independent of where the action takes place, cannot initiate actions with a limb. This has been called "motor neglect" by Laplane and Degos (4), but since this is not truly a motor disorder we prefer the name limb akinesia. The affected limb is usually contralateral to an injured hemisphere, and limb akinesia might be associated with frontal, parietal, or deep (e.g. thalamic) brain lesions. When present, limb akinesia is more commonly associated with right than left hemisphere lesions (5). Clinically, limb akinesia might look like a hemiplegia. However, patients with hemiplegia, when asked to move an affected limb, usually have some movement of the affected side such as elevation of the shoulder. Patients with akinesia, however, might not move anything and might not even appear to be exerting any effort. In addition, these patients might have anosognosia or unawareness of hemiplegia (6). They might be unaware of their hemiplegia because they do not attempt to move their arm. If patients do not try to move, they might be unaware that they cannot move (7). In many cases, however, the diagnosis of limb akinesia versus weakness from injury to the corticospinal tract must rely on structural imaging which demonstrates that the injury did not involve motor areas or physiological techniques such as motor evoked potentials, as described above. In some cases, a limb akinesia might co-occur with a hemiplegia. In these cases, it is difficult to know how much of a patient's disability results from damage to the corticospinal system and how much results from an akinesia. Taub and his associates (8) found that, in patients with a hemiplegia, restraining the good arm and thus forcing the patient to use the impaired arm might help reverse the weakness. While this has not been systematically studied, the restraint type therapy described by Taub *et al.* (8) might influence limb akinesia in patients with combined deficits more than it helps their corticospinal disorder. Since motor neglect is more commonly associated with right than left hemisphere injuries one might expect that non-use of the left arm would be more likely to benefit from Taub's therapeutic method than non-use of the right arm.

3.3.1.2. Eye and Head Akinesia

The eyes and head might also be akinetic. In these body parts, however, the akinesia is almost always specific for direction or action space and hence will be discussed in the next section.

3.3.1.3. Whole Body Akinesia

Patients with right hemisphere lesions and neglect might demonstrate an akinesia of both sides of their body. The ipsilesional akinesia is usually less severe than the akinesia on the contralesional side, but overall these patients make less movements than do normal people and this whole body akinesia might account for their increased risk of pneumonia, decubiti and thrombophlebitis.

3.3.1.4. Motor Extinction

Patients with sensory extinction to double simultaneous stimulation may be able to feel single stimuli on their contralesional body. When these patients, however, are presented with a simultaneous (distracting) stimulus on the ipsilesional side, they may then be unaware of a contralesional stimulus. One of the explanations for sensory extinction is that these patients have a diminished attentional capacity with an ipsilesional attentional bias. Thus, the presence of multiple stimuli overwhelms this limited capacity system. Since impaired intentional systems also might have a reduced capacity to manage multiple outputs, to test for milder forms of limb akinesia one can use a "motor extinction" paradigm. For example, Valenstein and Heilman (9) reported a patient who could make unilateral movements with either arm and did not have sensory extinction. However, when asked to make bilateral simultaneous movements, he either did not move his contralateral arm or moved it only after a prolonged delay. Viader *et al.* (10) reported similar observations.

3.3.2. Action Space

3.3.2.1 Directional Akinesia

Akinesia of the limbs, eyes, or head may depend upon where in space the body part is located or in what direction it is moved. Like attentional neglect or inattention, there may be a hemispatial or directional component to the akinesia. For example, patients with large hemispheric strokes often demonstrate gaze deviation toward the injured hemisphere. Although this has been called a gaze palsy, because very strong contralesional stimuli or vestibulo-ocular reflexes can induce contralesional eye movements, this is more consistent with a gaze preference or a directional akinesia rather than a gaze palsy. The ocular directional akinesia, like many of the deficits we will be discussing, is more common after right than left hemisphere lesions (11). Some patients with a directional ocular akinesia also have their head turned in the same direction, an oculo-cephalic directional akinesia. While not as apparent, a similar phenomena can be seen in the forelimbs. For example, if patients with unilateral right hemisphere lesions are asked to close their eyes and to point to a place in the room that is directly opposite their body midline, some will point, in error, toward the side of the hemispheric lesion (12). They move their arm toward ipsilateral (e.g., right space) because they have a bias to make movements toward ipsilateral (right) space, and/or a

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disinclination to make movement toward contralesional (left) space.

3.3.2.2. Hemispatial akinesia

Hemispatial akinesia is a failure to move a body part, such as an arm, in contralesional (e.g., left) hemispace (13). This disorder is unlike directional akinesia because it is not direction (e.g., leftward) specific. Thus, if the contralesional (e.g., left) arm is held in contralesional (e.g., left) hemispace the patient has trouble moving the arm to either side. However, when the arm is held in ipsilateral (e.g., right) hemispace, the patient can move it in either direction. The degrees of akinesia, such that independent of direction of movement, an arm may move less in contralesional (left) hemispace than in ipsilesional (right) hemispace. A directional akinesia might also interact with hemispatial akinesia. We do not know if hemispatial akinesia that is completely independent of direction has been described for the eyes or head.

3.3.2.3 Spatial Akinesia and Unilateral Spatial Neglect

When patients with unilateral or hemispatial neglect are asked to perform a variety of tasks in space, they neglect the hemispace contralateral to their lesion. For example, when asked to draw or copy a picture of a house or flower, they may draw only the ipsilesional half. When presented with a line and asked to find the middle, their attempted bisection mark might deviate toward the injured hemisphere. When asked to cancel stimuli in an array, such as letters, they may fail to cancel the stimuli contralateral to their hemispheric lesion. Early investigators of the neglect syndrome, such as Poppelreuter (14), suggested that this disorder might be induced by inattention or unawareness of stimuli in contralesional hemispace. More recently, other investigators have suggested that there is an ipsilateral attentional bias or an inability to disengage from ipsilateral stimuli (15, 16). Watson, Miller and Heilman (2) suggested that a failure to explore or act in or toward contralesional hemispace could also induce this deficit and dissociated attentional and intentional neglect in monkeys using the crossed response task. Based on their work, Coslett and coworkers (17) wanted to learn if intentional as well as attentional deficit could induce unilateral spatial neglect in human patients. To dissociate intentional deficit (hemispatial akinesia) from hemispatial inattention, Coslett *et al.* (2) had patients bisect lines while viewing the lines, and their own responding hand, on a TV monitor. Patients were prevented from viewing their hand or the line directly. Both the line (where the action takes place) and the TV monitor were independently placed in either ipsilesional (e.g., right) or contralesional (e.g., left) hemispace. A greater ipsilesional (e.g., right) bias of line bisection with the TV monitor in contralesional (e.g., left) as compared with ipsilesional (e.g., right) hemispace, independent of line placement, indicates hemispatial inattention. A greater ipsilesional (e.g., right) bias of line bisection when the line is placed in contralesional (e.g., left) hemispace as compared with ipsilesional (e.g., right) hemispace, independent of monitor placement, suggests a primary contribution of a hemispatial akinesia. Coslett and coworkers (17) found that there were patients who appeared to have primarily attentional neglect and others

who had a hemispatial akinesia. The patients with inattention had primarily temporal-parietal lesions, and those with hemispatial akinesia had primarily frontal lesions.

Bisiach *et al.* (18) also attempted to learn if directional akinesia (a reluctance or failure to move in a contralesional, (e.g., leftward) direction versus contralesional (left) spatial inattention could induce neglect. They had subjects perform a line bisection task by moving an arrow on a circular string that was aligned with the line to be bisected. The string ran over two pulleys on each end of the paper that contained the line. When the subject moved the portion of the string that was on top (the direct or congruent condition), if the patient erred by locating the arrow to the ipsilesional side of the actual midline (e.g., right sided bias), this could be related to either inattention to the contralesional (e.g., left) half of the line or a contralesional (leftward) directional akinesia. When the subject guided the arrow by moving the bottom string, because moving the string in one direction moved the marking arrow in the opposite direction (indirect or incongruent condition), if the patient had sensory neglect the patient's performance should be no different than when the upper string was moved. If, however, when the subjects used the upper string (direct condition) and demonstrated a rightward bias, and this bias was caused by a directional akinesia, then when the subject guided the arrow by moving the lower string (indirect condition) and failed to fully move leftward, the arrow would then be displaced more to the left than it was in the upper string/direct condition. Six of 13 subjects in this study showed a significant reduction of neglect in the incongruent condition, suggesting that they had a significant motor-intentional bias. These patients also had predominantly frontal lesions.

Na and coworkers (19) attempted to dissociate attentional and intentional aspects of neglect by having subjects view their performance of a line bisection task on a video monitor. Subjects could not view the workspace directly. A video camera displayed the workspace on the monitor either normally, or right-left reversed (by rotating the camera 180 degrees). If neglect were primarily attentional, the subjects' performance would be influenced by the visual feedback supplied by monitor display of the task. Thus, one would expect that when the monitor image is not reversed, the subjects with attentional neglect would perform as they perform on the usual bedside line bisection test (err to the right of center). When, however, the image is right-left reversed, subjects would reverse the direction of line bisection error, because in this condition the left side of the screen has the portion of the image from actual right hemispace and visa versa. These subjects would thus err leftward when viewing a reversed image. In contrast, the performance of patients with intentional spatial neglect should not be primarily influenced by reversed feedback and they should continue to err to the right of center, even though on the monitor this is displayed as a leftward bisection. This technique allows investigation of the relative contribution of attentional and intentional biases in the same subject. For example, if a patient reverses their

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deviation in the reversed-display condition, but the deviation is less than it was in the normal display condition, this suggests an attentional bias, with some lesser contribution of a rightward intentional bias. Using this apparatus, Na *et al.* (20) found that most patients with spatial neglect had both intentional and attentional biases, but in patients with frontal lesions the intentional bias dominated and in patients with temporal-parietal lesions the attentional bias predominated. As we will discuss later, the finding of mixed attentional and intentional bias is consistent with the idea that the networks subserving attention and intention are closely associated and influence one another.

3.3.3. Approach and Avoidance Responses and Neglect

3.3.3.1. Ipsilateral Neglect or Approach Spatial Neglect

Many patients with frontal lesions demonstrate a manual grasp reflex. When an object touches these patients' hands, they automatically grasp the object, like normal infants. In addition, when asked to completely relax their forelimbs, patients with frontal and subcortical disease move their hand along with the examiner's hand or finger even when they are not grasping the examiner's hand or fingers. This phenomenon is called "mitgehen," from the German word that means "going with." Denny-Brown and Chambers (21) proposed that whereas normally, the parietal lobes mediate an approach response, the frontal lobes mediate an avoidance response. Thus, with frontal injury, because the frontal injury released the parietal lobes, the subject would demonstrate inappropriate approach behaviors. He noted that patients with frontal lesions show another neurological sign: an automatic reaching for objects that they see. He called this phenomenon magnetic apraxia. Guitton *et al.* (22) noticed that patients with bilateral frontal lesions had difficulty in suppressing reflexive glances at novel but non-target stimuli which would interfere with their generating goal-directed saccades. This phenomenon has been called the visual grasp. Subsequently Butter and coworkers (23) studied a patient with a right frontal lesion by having the patient make a saccade to finger movements. Initially after his stroke, if the patient was asked to look at a moving finger in either left or right head/body hemispace while fixating in the midsagittal plane, and the examiner moved a finger in left hemispace, the patient failed to saccade leftward. However, he could saccade rightward toward finger movement in right head/body hemispace. Based on the site of the lesion, this failure to generate leftward saccades could not be explained by a hemianopia. Thus, the failure to saccade to the left could be related to either left hemi-inattention (the patient was not aware of the stimulus), or an ocular directional akinesia. To dissociate these two possibilities, the investigators performed a crossed response task (2). The patient was asked to look left when he saw finger movement on his right side, and to look right when he saw left finger movement on the left side. To left-sided finger movement the patient was able to look right, but to finger movement on the right side the patient could not move his eyes left. This suggested that the patient had a leftward ocular directional akinesia. After a few weeks, the patient was tested again, using the ocular crossed response task. This time, when the examiner moved his finger in the

patient's right hemispace and visual field the patient had no difficulty making a saccade to the left, suggesting that the ocular directional akinesia had resolved. When the examiner, however, moved his finger in the patient's left hemispace and visual field, the patient invariably generated a leftward saccade, toward the stimulus, before looking, correctly, to the right. This suggested that the patient had an unilateral visual (ocular) grasp.

Kwon and Heilman (24) reported a patient with a right frontal lesion who not only had a left sided visual (ocular) grasp but demonstrated a similar phenomenon on sequential line bisection tasks. Initially after his right frontal stroke, this patient showed a right sided bias (left-sided neglect) on line bisections. After about a week, however, the patient's line bisection performance changed: he exhibited a left sided bias on line bisection tasks. These investigators termed this phenomena "ipsilateral neglect," and this disorder has also been called "ipsilesional neglect." Ipsilateral neglect could have at least two possible mechanisms. It could be induced by attentional grasp, such that the patient attends primarily to the contralesional (e.g., left) portion of the line. Ipsilateral neglect could also be an asymmetrical or hemispatial form of magnetic apraxia, such that the patient has a propensity or inclination to reach toward objects (e.g., the line segment) in the contralesional (e.g., left) portion of space. To dissociate these possibilities, Choi and his coworkers (25) used the video apparatus of Na *et al.*, (19) described above. This apparatus displays the line to be bisected on a monitor either normally, or right-left reversed. If neglect were primarily attentional, the subjects' performance would be influenced by the monitor display of the line, and one would expect that when the monitor image was right-left reversed, subjects would reverse the direction of line bisection error. In contrast, the performance of patients with ipsilateral intentional spatial neglect should be influenced primarily by the motor aspects of the task, and they should continue to bisect the actual lines toward contralesional (e.g., left) hemispace even in the image-reversed condition. They found that some patients with ipsilateral neglect had an intentional bias suggesting that their error on line bisection was related to an aberrant approach response and others had an attentional bias..

Robertson *et al.* (26) suggest that ipsilateral neglect may be a compensatory response for contralesional neglect, but Na *et al.* (27) demonstrated that acute processes such as selective hemisphere anesthesia can also induce ipsilateral neglect. Na *et al.*'s results, however, do not preclude the possibility that in some patients ipsilateral neglect could be related to a compensatory response.

3.3.3.2. Avoidance Spatial Neglect

As mentioned above, Denny-Brown (21) thought that while the frontal lobes mediate avoidance behaviors, the parietal lobes mediate approach behaviors. After damaging the parietal lobe of monkeys, he demonstrated that when he stimulated their contralesional (e.g., left) hand, instead of grasping the stimulus the animals would move their hand away from the stimulus (personal communication). He called this sign the manual avoidance response.

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After right parietal injuries, when asked to bisect lines, patients often err by placing their mark to the right of the actual midline. As discussed above, this error has been attributed to both attentional and intentional biases. Kodosi and Heilman (28), however, assessed a patient with left sided neglect from a large right hemisphere stroke for the avoidance response. As in the procedure used by Na. *et al.* (19), the patient was prevented from seeing the line and her hand by a drape and had to watch them on a TV monitor. In the Na procedure, a digital editor either does not rotate the line (direct condition) or in the reverse or indirect condition it rotates the line 180 degrees. In this study, the line which is horizontal in work space was rotated 90 degrees on the monitor so that it appeared to be vertical (e.g., aligned with the midsagittal plane). The patient also was asked to bisect lines that were vertical (radial and in the midsagittal plane) in actual work-space and displayed on the monitor as horizontal. In the usual horizontal condition the patient demonstrated a right sided bias in both the direct and indirect conditions suggesting that the patient's right sided bias was not being induced by inattention, but probably was related to an intentional directional bias (see above). In the indirect condition, the bias was greater than in the direct condition, and in this indirect condition, unlike the direct condition, the patient sees her hand on the left. Thus, seeing an image of her hand on the left might have increased an avoidance response. In the vertical feedback condition, there is no hand or line seen on the left. If this patient's right sided bias in the horizontal condition was purely an intentional bias, the bias should have been present even with vertical feedback, but it was not. In this condition the absence of a bias provides support for the hypothesis that this patient's right-sided bias was being induced by an avoidance response.

3.3.4. Exogenously-evoked motor activation, versus endogenously-evoked activation

Movements can be produced in response to an external stimulus or they can occur in the absence of an external stimulus. We term those movements which are in response to a stimulus exogenously-evoked motor activation (exo-evoked), and those that appear to be spontaneous, endogenously-evoked activation (endo-evoked). A patient may have both exo- and endo-evoked akinesia, which we term mixed or global akinesia.

When testing for akinesia, the clinician may want to assess the various body parts discussed and to learn if the akinesia is directional and/or hemispatial. To determine if someone has endo-evoked akinesia, the clinician has to observe spontaneous behavior or the lack of it. Patients with endo-evoked akinesia, in spite of having reduced spontaneous activity, may respond better to external stimuli. For example, some patients with neglect might not spontaneously move their eyes toward or in contralesional (e.g., left) hemispace, but when directed to move their eyes or when given a compelling stimulus in contralateral hemispace, they might move their eyes.

De Renzi *et al.* (29) developed a task that can be used to test for endo-evoked directional limb akinesia. In our modification, a patient is blindfolded and small objects

such as pennies are randomly scattered on a table in both body hemispatial fields within arms' reach. The patient is asked to retrieve as many pennies as possible. The task is considered endo-evoked because the patient cannot see the pennies and must initiate exploratory behavior in the absence of an external stimulus. Patients with an endo-evoked directional akinesia of the arm may fail to move their arm fully into contralateral hemispace and explore for pennies.

When a patient has good strength and spontaneously moves, but fails to move to a specific stimulus, the failure to move in response to a stimulus is often attributed either to an elemental sensory defect or to sensory inattention or sensory neglect. While sensory defects and sensory neglect may be responsible for a failure to respond, exo-evoked akinesia is often confused with sensory defects and sensory neglect. The basic testing method used for dissociating sensory defects and sensory neglect from exo-evoked akinesia (motor neglect) is the crossed response task (2), which we discussed above.

3.3.5. Hypokinesia

Many patients with defects in their intentional systems may have only a mild defect and these patients may not demonstrate complete inability to initiate a response (e.g., akinesia). Instead, their intentional disorder may only become manifest by a delay in initiating a response. We have termed this delay hypokinesia. This hypokinesia may be defined in a manner similar to the akinesia. Since the reaction time paradigm is required to detect hypokinesia, we cannot divide hypokinesia into exo- and endo-evoked types.

The same paradigms that are used to test for akinesia of the eye and limbs can be used to test for hypokinesia. While some patients with hypokinesia have such markedly slowed initiation times, and hypokinesia can easily be detected, others have more subtle defects and reaction time paradigms may be needed to observe their defects. Reaction times can be slowed for a variety of reasons including impaired attention, bradyphrenia or hypokinesia. To detect hypokinesia, one should use simple reaction times that do not require cognition and, therefore, cannot be impaired by bradyphrenia. Similarly, in order to test for hypokinesia one has to use stimulus parameters that ensure that inattention cannot masquerade as hypokinesia.

Hypokinesia can be seen both in the limbs and eyes, and may be independent of direction or directionally specific. Thus, for example, Heilman *et al.* (30) had subjects with left sided neglect from right hemisphere lesions move a lever either to the left or right to imperative stimuli and found that independent of the characteristic of the stimuli the initiation of leftward movements was slower than the initiation of rightward movement, a directional hypokinesia. Hypokinesia can also be hemispatial such that the initiation of movements (reaction time) with the same limb may be slower in one (e.g., left) hemispace than they are in the other (e.g., right) hemispace (13).

3.3.6. Hypometria

When subjects make movements of a decreased

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amplitude, it is called hypometria. Hypometria may be directional, hemispatial or affect specific body parts such as a limb or the eyes. For example, as we discussed above, a patient with a right hemisphere lesion may at first be unable to saccade to the left. However, as the patient gets better, he or she may be delayed at initiating a leftward saccade, or may make multiple small (hypometric) saccades. Hypometria may also be related to representational and perceptual disorders which are not intentional deficits. Hypometria might be related to impersistence such that the patients prematurely discontinue their movement. This will be discussed in the next section.

4. MOTOR IMPERSISTENCE

4.1. Definition

Motor impersistence is the inability to sustain an act. It is the intentional equivalent to a loss of vigilance in the attentional domain. Like akinesia it can be associated with a variety of body parts including the limbs and eyes. However, it may include other body parts including the eyelids, jaw and tongue. Like akinesia it may also be directional (31) or hemispatial (32).

4.2. Testing and Subtypes

When testing for impersistence of midline structures, the clinician can ask the patient to keep his or her eyes closed for 20 seconds. Alternatively one can ask patients to keep the mouth open or protrude the tongue for 20 seconds. Patients who can successfully persist at these acts may be further taxed by asking them to persist at 2 movements simultaneously. For example, they may be asked to keep their eyes closed while also keeping their mouth open for 20 seconds.

Limb impersistence can be tested for by asking a patient to maintain a posture such as keeping an arm extended for 20 seconds. Since limb impersistence can be hemispatial (32), one may want to test each limb in its own and opposite hemispace. Hemispatial impersistence, in the absence of directional impersistence, has not been reported for the head or eyes, but this may be because it has never been tested in patients. One could ask a patient to sustain up (or down) gaze for 20 seconds while the eyes are directed either toward the right or left. If the patient could maintain gaze in one hemispace (e.g., the right) but could not in the other (e.g., left) it would suggest that the patient has hemispatial impersistence of the eyes. If a patient has a directional impersistence of the eyes, she or he might be unable to maintain gaze directed to either the right or left hemispace and, therefore, one may not be able to test for hemispatial impersistence. To test for directional impersistence of the eyes, one requests the patient to look either to the left or right for 20 seconds. A similar procedure can also be used to test the head for directional impersistence. Directional impersistence may be influenced by hemispatial factors such that directional impersistence is worse in one hemispace than the other. Directional impersistence has not been described with the arm.

Patients with directional impersistence usually have more difficulty in maintaining motor activation in

contralateral hemispace or in the contralateral direction. While all persistence tasks are exo-evoked as stated earlier, one can use a signal or instructions to initiate the activity and then withdraw the stimulus or one can let the stimulus persist throughout the trial. Except for one circumstance, patients' performance is better in the latter condition than it is in the former condition. The exception is when the stimulus and persistent action take place in opposite directions. For example, one could ask a patient to look to the left until she or he is instructed to stop. Alternately, the examiner could position one hand in the patient's right head/body hemispace, and tell the patient that when the examiner raises one finger the patient is to look to the left until that finger is lowered. In this case the patient might have more trouble sustaining leftward gaze, but under these conditions the inability to sustain gaze might be related to defective response inhibition rather than motor impersistence. Thus, sensory-attentional or motor intentional distraction may increase the sensitivity of the tests.

Motor impersistence may contribute to hemispatial neglect. Chatterjee, Mennemeier, and Heilman (33) studied a patient with a right hemisphere lesion with a line cancellation task. This patient primarily cancelled line targets on the right side of the page. Unlike normal subjects who cancel targets going from left to right on the page, many patients with left sided neglect from right hemisphere injuries cancel targets going from the right to left. Thus, when subjects fail to cancel targets on the left side of the page, their failure has been thought to be related to either inattention to the left side of the page or a failure to act toward and in the left side of space. There is, however, another possible mechanism. It is possible that patients fail to mark or cancel items on the left side of the page because, after they start on the right side of the page, they prematurely quit, a form of motor impersistence. Chatterjee, Mennemeier and Heilman (33) asked this patient to first cancel an item on the right side of the sheet and then to cancel an item on the left side of the page. The patient was to continue this alternating right-left search until all the items were cancelled. Using this strategy, the patient's cancellations were no longer confined to the right side of the page. She did cancel many items on the extreme left side of the page, but now the targets on the center of the page were not cancelled. Unilateral inattention (unawareness) or a directional and hemispatial akinesia cannot explain these results, and one of the possible explanations of this woman's performance is that she quit prematurely, exhibiting motor impersistence.

5. DEFECTIVE RESPONSE INHIBITION: MOTOR ALLOCHIRIA AND HYPERKINESIA

There are two forms of defective response inhibition. In one form the ipsilesional limb moves when the correct response was a movement of the contralateral limb, or the eyes or head moved in an ipsilesional direction when the correct response was a movement in the contralateral direction. For example, after being trained in a crossed-response task, monkeys with neglect induced by frontal lesions appear to have motor rather than sensory

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neglect. We also found that the monkeys made more incorrect responses with the arm ipsilateral to the lesion than they did with the contralateral arm (34). The errors made by the ipsilateral arm could be a compensatory strategy or a disinhibition phenomenon. Because these incorrect responses were not rewarded and became more frequent as motor neglect improved, the incorrect responses of the ipsilateral arm are not a compensatory strategy, but rather a defect we term "ipsilesional disinhibition hyperkinesia" or "allokinesia." The avoidance response we discussed above might be a directional form of ipsilesional disinhibition hyperkinesia. This type of defective response inhibition may also be termed motor (limb or directional) allochiria (35). In patients, before one terms such a condition motor allochiria, one must be certain a perceptual problem has not induced the disorder. If the patient has a perceptual deficit, the behavior is not a form of defective response inhibition (disinhibition hyperkinesia) but is a true allochiria or allesthesia. In the second form of defective response inhibition, the contralesional limb moves when it should not move, or movement occurs in a contralesional direction when there should be either no movement or movement ipsilesionally. We will term this disorder contralesional disinhibition hyperkinesia, and this might be similar to the approach response associated with ipsilateral neglect that we discussed above.

6. MOTOR PERSEVERATION

Perseveration occurs when a patient incorrectly repeats a prior response. Although there are several classifications of perseveration (e.g., 36), most recognize that there is a spectrum between cognitive and motor perseveration. Cognitive perseveration occurs when one uses a previously used cognitive strategy inappropriately for a new or different task. For example, a patient performing the Wisconsin Card Sorting Test (37), after developing a strategy such as sorting by shape, may not alter this strategy even when instructed that it is inappropriate. Hence, these patients do not sort by some other criteria, such as color. Sandson & Albert (36) calls this form "stuck in set" perseveration. Luria (38) discussed two types of motor perseveration. In one type of motor perseveration the patient is unable to switch to a different motor program and repeats the prior program even though the task requirements have changed. Luria calls this inertia of program action and Sandson & Albert call this recurrent perseveration. In the second type the patient continues to perform a movement even though the task is completed. Luria called this efferent perseveration. This is similar to Sandson & Albert's (36) continuous perseveration. Continuous and recurrent perseveration might be induced by different defects in the "when" or intentional system. One deficit (recurrent) is knowing "when" to switch and the other (continuous) is knowing "when" to stop a motor program.

When performing a cancellation task, patients with motor perseveration might repeatedly cancel the same target. Na and his coworkers (20) studied motor perseverative behavior during line cancellation tasks in 60 patients with left hemispatial neglect from right

hemispheric strokes. More than 30% of the patients showed motor perseveration: repetitively canceling the same target, or canceling extra lines that they themselves added to the array. Neglect severity correlated positively with the frequency of perseverative errors. Perseveration was most prominent in the rightmost portion of the array. Anterior lesions were more likely to be associated with motor perseveration than were lesions restricted to the posterior areas. Because the degree of perseveration correlated with the degree of neglect, it is possible that the perseverative behavior prevented these patients from disengaging from the right most portion of the stimulus array. Hence, perseveration might have contributed to their neglect. Further studies must be performed to test this hypothesis.

7. PATHOPHYSIOLOGY OF INTENTIONAL DISORDERS

7.1. Right - Left Asymmetries

People can make almost every type of movement, and can make these movements at almost any time. Thus, cognitive movement programs have to provide the motor system with instructions. In general, there are two major types of cognitive-motor programs that control the motor system: the praxis programs and the intentional programs. The praxis programs provide the spatial, temporal and force instructions. In contrast, the intentional programs provide "when" instructions, such as when to move, when to persist at an action, when not to move and when to stop moving. In right-handed people, disorders of the praxis production system, as evidenced by ideomotor apraxia, are almost always associated with left hemisphere dysfunction (39). Intentional disorders, however, are frequently associated with bilateral hemispheric lesions. When the lesions associated with intentional disorders are unilateral, they are more commonly associated with right than left hemisphere lesions. For example, Coslett & Heilman (5) showed that contralateral limb akinesia occurs more frequently after right than left hemisphere lesions. The akinesias associated with right hemisphere dysfunction are frequently not limited to the left limbs. Howes & Boller (40), using a reaction time paradigm, reported that right hemisphere infarctions are associated with a greater slowing of reaction times (hypokinesia) than are left hemisphere infarctions even when the ipsilesional arm is used and lesions are matched for size. Rehabilitation specialists have noted that it is more difficult to rehabilitate patients with left than right hemiplegia. In addition, patients with left hemiplegia are more likely to develop decubiti, and venous thromboses with pulmonary emboli. Both of these conditions are promoted by overall inactivity associated right hemisphere dysfunction. Directional akinesia of the limbs as determined by tasks such as those used by DeRenzi *et al.* (29), and Heilman *et al.* (30) were also more frequently reported with right hemisphere lesions. The case of hemispatial limb akinesia reported by Meador *et al.* (13) had a right hemisphere lesion. Although impersistence is often associated with bilateral hemispheric dysfunction, when it is associated with unilateral hemispheric disease, it most commonly occurs after right hemisphere lesions (31). Defective response inhibition of

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the eyes or arms may be seen with bilateral hemispheric dysfunction, but, when occurring with unilateral hemispheric disease, it has been more commonly associated with right than left hemispheric dysfunction (41, 23). Lastly, motor (or continuous) perseveration has also been reported to be more frequently associated with right than left hemisphere dysfunction (36).

The lesion studies mentioned above suggest that, normally, the right hemisphere is dominant for "when" decisions or intentional control of the motor systems. This evidence, however, is indirect. There are two studies in normal controls which provide converging evidence for right hemisphere intentional dominance (42, 43). In these studies, normal subjects received warning stimuli directed to either the left or right hemisphere. The warning stimuli provided information about which hand would be called on to respond when an imperative stimulus appeared. Valid warning stimuli reduce reaction times because they activate motor systems in preparation for a movement. Using a reaction time paradigm, Heilman & Van Den Abell (42) demonstrated in normal subjects that warning stimuli projected to the right hemisphere reduce reaction times more than warning stimuli projected to the left hemisphere. Warning stimuli directed to the right hemisphere reduced left hand reaction times more than warning stimuli directed to the left hemisphere reduced right hand reaction times. More striking, however, valid warning stimuli to the right hemisphere even reduced right hand reaction times more than did warning stimuli directed to the left hemisphere. This provides strong support for the right hemisphere intention dominance postulate. This asymmetry might also help account for the observation that intentional neglect is more commonly seen with right than left hemisphere lesions. After left hemisphere lesions, the right hemisphere might be able to activate the ipsilateral limbs as well as movements in and toward ipsilateral hemispace. In contrast, after right hemisphere lesions, the left hemisphere can activate the right sided limbs as well as movements in and toward right hemispace, but cannot activate the ipsilateral limbs or movements in or toward ipsilateral hemispace.

While these studies in brain injured and normal subjects demonstrate right hemisphere superiority for intentional processes, we do not know the brain mechanisms that account for these asymmetries. Intention is closely linked to motivation. Herbert Spencer's biological theory of hedonism might still be the best guide for understanding motivation. According to this theory, pain is the correlative of actions that are injurious to the organism and pleasure is the correlative of actions that are conducive to the organisms welfare. Thus, normal animals seek pleasure and avoid pain. In humans there are at least 3 major motivational systems: the primary drive systems, the emotional systems, and the executive-cognitive systems.

The primary drive systems monitor the internal milieu (e.g., blood glucose) and when there is a deficiency state (hypoglycemia), or an absence of homeostasis, the organism has unpleasant or painful sensations (e.g., hunger) that induce goal-oriented behavior (e.g., eating). When the

goal is being achieved and homeostasis is being re-established, there are pleasant sensations. In normal circumstances (e.g., in the absence of mood disorders) the emotional systems are activated by external stimuli (e.g., a snake or a puppy). Based on either the nature of the stimulus or the interpretation of stimulus significance, positive or negative emotions are evoked. Positive emotions (e.g., happiness, satisfaction) are internal sensations or feelings that are associated with stimuli that are conducive to the organism's welfare and negative emotions (e.g., fear and anger) are associated with stimuli that are either directly injurious to the organism or foretell possible injury. These positive or negative feelings provide the organism with goals.

The executive-cognitive systems contain knowledge of the environmental circumstances that may be either conducive or injurious to the welfare of the organism and, hence, may produce future pain or pleasure through the primary drive or emotional systems. Therefore, even in the absence of primary drives or emotions that induce pain or pleasure, the organism's desire to avoid pain and seek pleasure ensures that its action is directed toward the appropriate goals.

There has been much written about these three motivation systems, but knowledge of their anatomic and physiologic bases is far from complete. Primary drives appear to be mediated by the diencephalic-limbic systems (e.g., hypothalamus), emotions are mediated by limbic (e.g., amygdala) and cortical systems, and executive programs by the neocortex (e.g., frontal lobes). Since the primary purpose of this paper is to discuss intentional systems, we will not fully review this work. Although the anatomic and physiological basis for the right hemisphere's special role in intentional activity is unknown, the limbic system, which plays a critical role in motivation, has two major outputs to the cortex, one from the hippocampus and the other via the cingulate gyrus. While medial temporal lobe (e.g., hippocampus) lesions are associated with profound amnesia, severe motivational or intentional disorders have not been associated with these lesions. In contrast, medial hemispheric lesions that involve the cingulate gyrus or its connection to the neocortex are associated with intentional disorders suggesting that the cingulate gyrus provides motivational information to neocortical areas. Eidelberg & Galaburda (44) demonstrated that the right cingulate gyrus has more input into the neocortex than does the left, and this asymmetrical input might, at least in part, account for the right hemisphere's dominance in intention.

Hemispheric asymmetries of intention might be based on neuro-transmitter asymmetries. Reduced dopamine, as seen in Parkinson's disease, is associated with akinesia and increased levels of dopamine can induce hyperkinetic disorders. When rats are given dopamine agonists, they demonstrate rotatory behavior. On post-mortem examination, these animals have higher levels of dopamine in the hemisphere that is contralateral to the direction of rotation (45). Mohr *et al.* (46) gave L-dopa to normal right handed subjects, blindfolded them, had them

walk and noted that they deviated to the left, suggesting that their right hemisphere may have had higher levels of dopamine than did their left hemisphere.

7.2. Intrahemispheric Networks

Studies of patients and monkeys with focal lesions suggest that the frontal lobes play a critical role in intentional activity. The frontal cortex has strong projections to the basal ganglia (e.g., the striatum). The dorsolateral frontal lobe projects to the caudate, the supplementary motor area projects to the putamen, and the cingulate gyrus projects to the ventral striatum. The striatum projects to the globus pallidus interna, and the pars reticularis of the substantia nigra, and these basal ganglia project to thalamic nuclei (e.g., VA, VL, MD). These thalamic nuclei project back to the same area of the frontal cortex where they originated.

Intentional disorders, such as akinesia, may be associated with diseases that affect both the basal ganglia and regions of the thalamus. Diseases that affect the white matter that connects the frontal lobes with these subcortical structures can also induce intentional disorders. Akinesia has also been reported with temporo-parietal lobe lesions (47, 3). While the akinesia associated with basal ganglia diseases such as Parkinson's disease appears to be endo-evoked, the akinesias associated with frontal and parietal cortical dysfunction appear to be exo-evoked (2, 47).

The frontal lobes might play a central role in directing intentional activities because of its connections. The dorsolateral frontal lobes receive projections from both the inferior parietal and posterior temporal lobes, which are polymodal association cortex. It also receives projections from modality-specific association areas. The frontal lobe has strong reciprocal connections to the cingulate gyrus, the dorsal-medial thalamic nuclei, and non-reciprocal connections with the striatum as previously described. The frontal lobe's connections with the inferior parietal and posterior superior temporal lobes may provide the frontal lobe with stored knowledge (cognition) about the meaning of stimuli and the strategies for dealing with the environment. The limbic connections may provide the frontal lobe with information about primary drives and emotional information. The confluence in the frontal lobes of cognitive information together with knowledge of conditions that induce emotions and primary drives make the frontal lobes well suited to direction intention.

Physiological studies have provided converging evidence for the role of the frontal lobes in mediating intentional-motor activation. For example, Suzuki and Azuma (48) recorded from neurons in the dorsolateral frontal lobe of monkeys who were trained to make a rapid movement to a stimulus. When the animal was prepared to make a movement, the cells were active. When the animal was not prepared to initiate a response, however, these cells' activity was reduced. Stimulus parameters did not affect these cells' activity, suggesting that these cells are intentional neurons important in preparing the animal for action.

We do not know if the different forms of intentional activities we have discussed are mediated by the same network or different systems. Some of the intentional disorders we discussed may be related to an inability to activate motor systems, while others might be due to the "release" of phylogenetically more primitive motor control systems. For example, Goldberg & Bushnell (49) demonstrated that neurons in the dorsolateral frontal lobes have a role in the preparation for saccadic eye movements. Based on Goldberg & Bushnell's work, one would predict that injury to these cells on one side would induce a directional akinesia of the eyes such that these animals could not make contralesional saccades. While Goldberg & Bushnell (49) demonstrated that neurons in the dorsolateral frontal lobe have a role in preparing for a saccade, superior collicular neurons can perform a similar function. After frontal lobe damage (e.g., right) initially there is a directional akinesia such that saccades can not be made in a contralesional (e.g., leftward) direction, but the ability to make saccades returns and this recovery is probably mediated by the colliculus. The activity of the colliculus, however, unlike that of the frontal lobes, cannot be altered by task instructions or cognitive set. Normally the dorsolateral frontal lobes might exert an inhibitory influence on the superior colliculus which is absent after frontal lesions, such that the person is unable to inhibit making reflexive saccades to moving stimuli (visual or ocular grasp). A similar release of inhibition may also be responsible for other non-ocular defects causing the brain-damaged patients to have difficulty either withholding or terminating responses.

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