An Introduction To The Higher Cerebral Disorders In Man

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IN MEMORY OF NORMAN GESCHWÎND 1926- 1984

Norman Geschwind, James Jackson Putman, Professor of Neurology at Harvard Medical School and Chief of the Neurology Department of the Beth Israel Hospital, died suddenly and unexpectedly of a massive heart attack on November 4, 1984, at the age of 58. Geschwind was born in New York in 1926. He received an MD degree from Harvard in 1951. He spent three years at the National Hospital in Oueen Square, London on a U.S. Public Health Service Fellowship. In 1955, he returned to the U.S. as Chief Resident in the Neurological Unit of the Boston City Hospital, under the directorship of Denny Brown. In 1963, he became Chief of the Neurology Service at the Boston V.A. Hospital. In 1966, he established the Aphasia Reserach Center. In 1969, he accepted the James Jackson Putnam Chair at Harvard Medical School. He was also appointed Professor of Psychology at the Massachusetts Institute of Technology in 1978. During the several years immediately preceding his untimely death, he was involved in writing a major monograph synthesizing the interaction among the processes of latéralisation, autoimmunity, and sex hormones. Fortunately, he did complete a first version of this work. His loss will be felt by a host of followers throughout the world who owe him their enthusiams for behavioral neurology.

I. HEMISPHERIC DOMINANCE

One of the most fundemental aspects in the anatomic organization of function is the marked hemispheric differences in behavioral specialization. Whereas primary sensory-motor function are equally distributed between the two sides of the brain, the control of more complex functions is markedly asymmetrical in organization. Hemispheric asymmetry is probably the most fundemental biologic hallmark of human cerebral evolution.

First of all, the left hemisphere is both necessary and sufficient for language functions in the overwhelming majority of individuals. Thus, it becomes important that many cases of right hemiparesis due to left hemisphere disease may have different types of language dysfunction. Indeed, it is very difficult to find nonaphasic cases with the left hemisphare involvement in the clinical practice. Left hemisphere dominance for language is the rule for right-handed individuals; it is sometimes stated that as many as 99% of those who prefer the right hand for writing and other motor activities have dominance for language in their left hemisphere. (18) Among left-handed individuals some investigators suggest a 60/40 left/right split. Crossed aphasia, the occurence of aphasia in a right-handed individual following right hemisphere damage is relatively rare which is usually estimated as 1% among the right-handed population. (22)

Hemispheric dominance for language is a strongly laterlized neural function.

In contrast to the dominant function of the left hemisphere, the specializations of the right hemisphere did not gain widespread acceptance until much later. Although there are still different controversies on detail, it is now generally accepted that the right hemisphere in most dextrals is specialized for at least four major areas of behavior: 1) complex and non-linguistic perceptual tasks, including face identification; 2) the spatial distribution of attention; 3) emotion^ behavior; and 4) paralinguistic aspects of commungfltion.

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The behavioral syndromes due to neurological diseases (neurobehavioral syndromes) can be analysed by means of anatomical aspects and the syndrome characteristics. Regarding with the anatomical aspects there are three distinct patterns: 1. Neuro-behavioral syndromes due to left hemisphere disase. 2. Neuro-behavioral syndromes due to right hemisphere disease. 3. Neuro-behavioral syndromes due to bihemispheric diease.

1. NEUROBEHAVIORAL SYNDROMES DUE TO LEFT HEMISPHERE DISEASE :

A. Language Disorders: Aphasias can be defined as loss of Language functions due to dominant (left) hemisphere involvement. [2] There are several types of aphasia. The most important anatomical substrate for the language functions is the perisylvian area including the parts of the frontal, temporal and parietal lobes cortically and subcortically. The well-known Broca's and Wernicke's areas, arcuate fasciculus, and angular and supramarginal gyri are located in this area. Despite the specific responsibilities each area on language functions, there is **a** close relationship between these areas. Let us consider how a child learns the language: First question would be how a child learns the name of a seen object. The child must link the name spoken by another individual to the visual image of the object. The name of a seen object can be heard by the primary auditory cortex (Heschl's gyrus) which is located on the anterior aspects of the superior temporal gyrus and is transmitted to Wernicke's area which is located on the posterior aspects of the same gyrus in order to be understood. On the other hand, the visual image of the object is received by the primary visual cortex (area 17) and is distributed to the visual association cortices (areas 18 and 19). In order to connect these two different informations, child has to have a specific anatomical relationship or area between two cortical areas. When the object is seen and the name is heard simultaneously, the angular gyrus acts to link the neural pattern of the visualized object to that of the heard word.

In the future, when the name is heard it is transmitted to Wernicke's are for recognition of the sound pattern of the word; this in turn arouses the angular gyrus, and a visual memory of the seen object is evoked. Wernicke's area and the angular gyrus are essential way-stations in the comprehension of certain aspects of spoken language. How does the child learn to say the name? When the child first hears a name, the appropriate neural pattern is transmitted from Wernicke's area to Broca's area via the arcuate fasciculus. Broca's area eventully acquires the rules for turning the heard work into spoken form. How does the child repeat the heard word? The arcuate fasciculus plays a crucial role in the repetition function. How does the child learn to read? The angular gyrus region plays a major role and is of central importance for reading comprehension. As writing depends on having learned to read, the angular gyrus is also essential for writing, yet there is considerable evidence about the role of the different anatomical regions in writing function. Figure 1 shows the important language areas of the dominant (left) hemisphere.

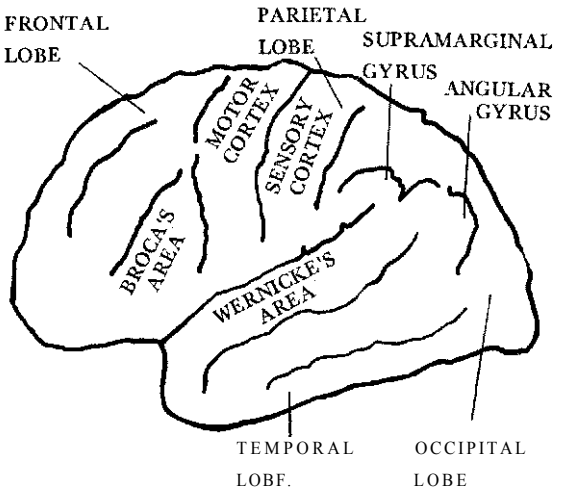

FIGURE 1 Lateral surface of the left cerebral hemisphere, showing the important speeceh areas in relation with the primary cortical areas.

In addition to the specific cortical areas, the association pathways and capsulostriatal areas of the hemisphere play important roles in language. Because of knowing the anatomical and clinical importance of the association pathway, one can easily differentiate the aphasias into two major syndrome complexes: Aphasias with repetition disturbance, and aphasias without repetition disturbance. Therefore, it may be very easy to localize the lesions outside or inside perisylvian areas: Aphasias with repetition problems (Broca's, Wernicke', conduction) can be localized into the perisylvian zone, while the aphasias without repetition problems (transcortical aphasias, some subcortical aphasias) can be localized outside the perisylvian region.

There has been increasing evidence about the role of subcortical areas on language functions within last two decades. There are two major anatomical areas in relation to the language functions. Dominant (left) thalamus, and left capsulostriatum. Regarding the left thalamus, ventral-lateral nucleus is heavily involved in language functions. [16] The main characteristics of the thalamic aphasia are fluent speech, nearly normal repetition and auditory comprehension, poor naming, and poor verbal

memory. Despite the borderline eases, the lesions of the left eapsulostriatum may produce two different types of aphasias: nonfluent aphasias with the lesions of the posterior limb and posterior aspects of the putamen. In addition to the anatomical and clinical differences with the cortical aphasias, these aphasisas usually show good recovery. [15, 19]

B. Apraxia : This is the inability to carry out a motor task, wihch cannot be explained by a basic neurologic disorder and. or aphasia. Despite the several theoretical classifications, apraxias can be classified into three major forms:

1) Ideomotor appraxia which is the inability to carry out a motor task involving the previously learned motor movements.

2) Ideational apraxia which is the inability to execute two or three motor acts subsequently.

3) Unilateral hand apraxia which is the inability to carry out a motor task with the hand unilateral to affected hemisphere. Figure 2 shows the anatomical basis of apraxias. Among the different types of apraxias, the first two indicate the involvement of the supramarginal gyrus and/or the perisylvian areas, while the latter indicates the involvement of the anterior portion of the corpus callosum.

C. /uexias : The disorders of reading comprehension can be classified into three forms: 1) Alexia without agraphia (posterior alexia)

2) Alexia with agraphia (central alexia)

3) The "third alexia" (anterior alexia)

1. Alexia without agraphia (posterior alexia): J.Dejerine was the first to describe this syndrome with the lesions of the left medial occipital lobe and the splenium of corpus callosum. [8] Because of these lesions visual information from both visual cortices can not reach to the angular gyrus of the dominant (left) hemisphere. Therefore, alexia without agraphia is considered to be a perfect sample of disconnection syndromes. Associated symptoms are important and may determine the specific patterns of the lesion localizations. Hemianopia itself may have a little localization value in terms of medial, basal or lateral lesion localizations, while color anomia (or agnosia) may indicate the specific involvement of the medial occipital lobe, and the presence of amnesia may indicate the involvement of the medial temporal lobe.

2. Alexia with agraphia (central alexia) : This was also described by Dejerine with the lesion of the left angular gyrus. [7] Writing disorder is almost always associated with the reading disorder. The syndrome can be seen as an isolated syndrome or as a part of Gerstmann's syndrome. It is totally different from the alexia without agraphia syndrome in terms of anatomical localization and clinical aspects.

3. The "Third alexia" (anterior alexia) : Disorders of reading comprehension with anterior lesions were mentioned in the older literature. It has been suggested that the reading impairment that occurs with anterior aphasia, particularly Broca's aphasia, is distinctive and can be called anterior alexia. The main characteristic of this type is the "letter alexia" with the relative preservation of the word reading.[3]

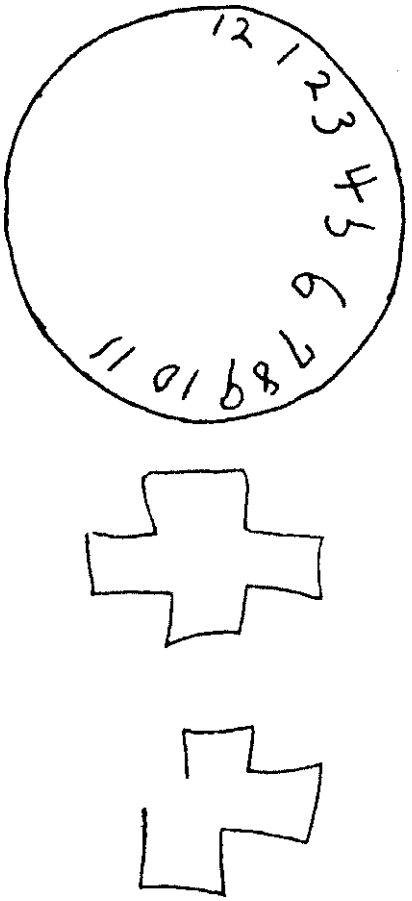

Figure 2. and Figure 3. Left hemispatial neglect in patients with the right panetal lesions.

D. Verbal Amnesia Dissociated verbal memory disorders have been described with the left hemisphere lesions. [5,14] These involve the immediate and short-term memory stages. Recently, we have been examining the unilateral stroke patients on different memory tasks involving the immediate, short-term (15-second delay) and long-term (15-minute delay) items. Our preliminary results have indicated that memory is dissociated after unilateral stroke into verbal and nonverbal forms. Aphasia appeared to be an important factor in memory disorder. Besides, there are a couple of areas in which the left hemisphere such as medial-dorsal thalamic nucleus, hippo-

campus, and possibly posterior language association cortices.

2. NEUROBEHAVIORAL SYDROMES DUE TO RIGHT HEMISPHERE DISEASE :

A. Right Hemisphere Lesions and the Complex Non-Linguistic-Visual Skills :

The performance of visuo-spatial tasks presupposes normal visual acuity, the ability to perceive the several elements of the model as well as their spatial relationship, and finally adequate motor ability. Failure in any of these elementary prerequisites can lead to impairment in these tasks, so that the constructional abilities of such patients could not be tested adequately. Patients with right hemisphere lesions tend to have dysfunctions of the lineorientation, construction and the recognition of unfamiliar faces. Defective performances in these tests are strongly correlated with posterior cortical lesions, though different subcortical lesions have been held responsible for these abnormalities. Although the constructional dysfunction has been considered to be a praxis problem, it is reasonable to say that the correlation between the constructional problems and visuo-spatial dysfunction is much more evident.

Stereopsis is the ability to discriminate depth on the basis of binocular visual information. It has been postulated that the right hemisphere is dominant for stereopsis. [4] Support for the hypothesis that stereopsis could be preferentially related to right hemisphere processing also came from some studies in normal individuals, in which random-dot stereograms were presented tachistoscopically, and performance in the left hemifield proved superior.

Nonverbal memory problems may be associated with the right hemisphere disease. [5] In addition to the previous studies, more recently, we have found significant correlations between the nonverbal memory impairment for figures and right sided lesions, whether or not the figures were verbalizable.

B. Disorders of Unilateral Attention (Neglect):

The right hemisphere contains the neural machinery for attending to both sides of the extra personal space, whereas the left hemisphere contains the machinery for attending to only the contralateral right hemispace. This leads to the emergence of marked contralateral neglect after right hemisphere injury but not after equivalent left hemisphere injury.

1. The parietal lobe and Neglect : Unilateral has been described in patients with lesions of posterior parietal cortex, lateral prefrontal cortex, thecingulate gyrus, the sitriatum, and thalamus. [13]Recent evidence, however, suggests that the neglect that results from parietal lobe damage alone may be quite subtle and that lesions in the superior rather than in the inferior parietal lobule may be more closely associated with neglect behavior. With respect to clinical features, patients with parietal lobe damage tend to have prominent multimodal extinction when presented with bilateral simultaneous stimulation, they neglect the internal sensory representation of the left extrapersonal space, and they have difficulty with leftward shifts of covert attention. Figure 2 and 3 show the samples of hemispatial neglect in patients with the right parietal lesions.

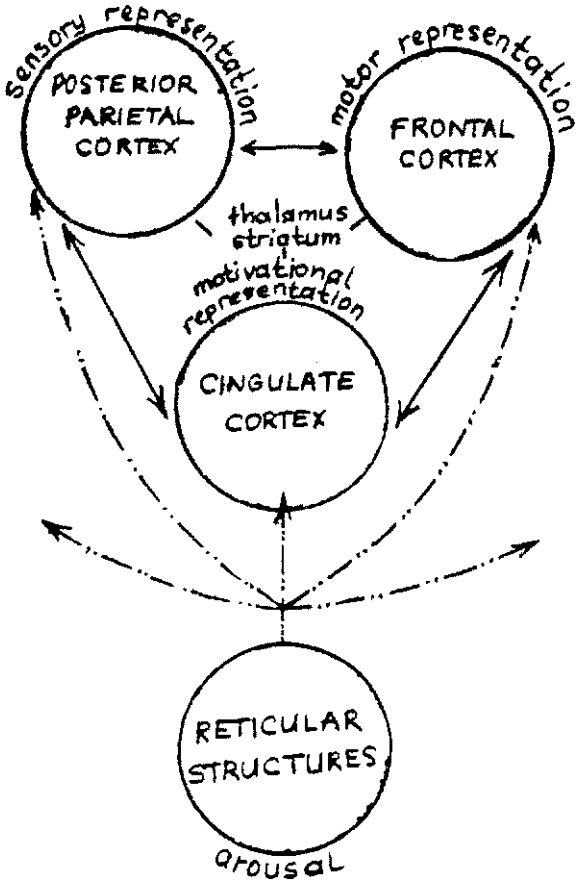

Figure 4. A network involved in the distribution of attention to the extrapersonal targets.

It has been possible to record the activity of single neurons in this part of the brain in awake and behaving animals. Neurons in the inferior parietal lobule, especially in its PG sector, have been shown to increase their firing rates when the animal detects, looks at, or reaches toward a motivationally relevant object such as food when hungry or liquid when thirsty. Area PG has remarkably selective connections,

which can be subdivided into the four major categories.

2. The limbic system in Neglect : It has been shown that area PG receives massive neural input from limbic areas including the cingulate gyrus, the retrosplenial area, and the nucleus basalis. In monkeys, unilateral lesions of the cingulum bundle and adjacent cingulate cortex result in contralateral somatosensory extinction. [20] In the human, medial frontal infarcts focused around the cingulate region of the right hemisphere have given rise to typical unilateral neglect syndromes for the left hemispace. [10] The limbic system of the right hemisphere is considered to represent the motivational aspect to the attentional mechanism.

3. The frontal lobe and Neglect : In both man and monkey there is a cortical area just rostral to premotor cortex in which stimulation results in contralateral head and eye deviation. This area has been called the frontal eye fieldes. Unilateral lesions that include the frontal eye fields can cause profound contralateral neglect in humans as well as in monkeys. [17] One might have expected that frontal neglect would have more of the motor components of neglect behavior, whereas parietal neglect would be characterized by a predominance of sensory features. Yet we do not have enough information to know if such distnictions can be made in the human.

4. Subcortical Neglect : Unilateral neglect in the human has also been observed after lesions of the thalamus. [21] It is not yet clear which of the many thalamic nuclei are responsible for the resultant neglect, yet the intralaminar thalamic nuclei are probably involved in this process. Unilateral striatal damage has also been associated with contralateral neglect in humans. [9] Interrupting the dopaminergic nigrostriatal pathway has also been reported to yield contralateral neglect in animals.

5. The reticular activating system and Neglect: The intralaminar thalamic nuclei, the brainstem raphe nuclei, the nucleus locus coeruleus project to area PG as well as to virtually all other parts of cortex. It is reasonable to say that this input regulates the overal attentional tone (arousal) in area PG as well as in other cortical regions. Figure 4 shows a network involved in the distribution of attention to extrapersonal targets.

C. Right Hemisphere and Emotion :

Clinical observations suggest that there may be consistent hemispheric differences in the emotional response to experience. For example, the lack of concern and even the inappropriate jocularity in response to hemiplegia is a striking feature of some right hemisphere infarcts, although it is almost never seen in patients with left hemisphere lesions. Regarding with the clinical experience, there is evidence showing that the right hemisphere is more closely associated with the expression of negative (dysphoric) emotins, whereas the left hemisphere seems to impart a more positive (euphoric) emotions. Further deficits in the encoding (display) of emotional expression are associated with lesions in the more anterior frontal parts of the right hemisphere, whereas more temporoparietal lesions tend to disrupt the decoding (under-standing) of emotional expressions. Thus, the neural subtrate for the encoding and decoding of affect shows a plan of organization that parallels the organization of language in the left hemisphere. There are also some indications that affective disease may be more closely associated with right hemisphere dysfunction. For example, it has been suggested that in temporolimbic epilepsy, left-sided foci are more likely to be associated with ideational disorders, whereas right-sided foci are more likely to be associated with affective disturbances. [1]

D. Right Hemisphere and Motor Impersistence

Motor impersistence is used to describe the inability to sustain simple acts such as conjugate gaze, keeping the mouth open, protruding the tongue, fixing the eyes centrally, holding the eyelids shut or turning away. It has been suggested that right hemisphere lesions caused more impersistence than equivalent left hemisphere lesions. [11] Apraxia and inattention have been held responsible for motor impersistence.

3. NEUROBEHAVIORAL SYNDROMES DUE TO BIHEMISPHERIC DISEASE :

A. Amnestic Syndromes :

Memory becomes disturbed in a great number of clinical conditions, ranging from metabolic encephalopathy, to head injury, tumor, epilepsy, cerebrovascular diseases, and dementia. The clinical and neurologic data lead to the formulation of a general rule : almost all severe amnesias occur after bilateral involvement of limbic structures.

1. Amnesias with bilateral limbic **involvement**

a. Medial **temporal** lesions : Bilateral temporal lobectomies, Herpes Simplex encephalitis, bilateral medial temporal infarcts and tumors have been described as a cause of amnestic syndrome.

b. Bilateral Limbic diencephalic lesions : Korsakoff's syndrome, hypothalamic and thalamic lesions are associated with severe amnestic syndrome. The lesions are always bilateral and symmetrical and always affect subcortical structures.

c. Basal forbrain lesions
d. Bilateral fornix lesions
e. Cingulate lesions

2. Selective Amnesias : Selective of unilateral amnesias have already been discussed in previous chapters.

3. Amnesias of unknown anatomy :
a. Closed head trauma
b. ECT
c. Epilepsy
d. Drugs
e. Huntington's disease
f. Depression

4. Transient Global Amnesia :

Transient global amnesia is a syndrome with various possible etiologies. It is conceivable that a common denominator is injury to the hippocampus and associated medial temporal structures.Ischemia in the territory of the posterior cerebral arteries is possible but difficult to prove. A thalamic infarct can initially resemble a transient global amnesia but does not lead to recovery. Migraine headaches also can cause transient global anmesia. An epileptic mechanism has been suggested as well, but this must be rare and has to be differentiated from epileptic fugue states.

5. Benign Senescent Forgetfulness :

This is an essentially indolent condition that does not progress to dementia. The greatest difficulty is for names and details, though events are easily recalled.

B. Agnosias :

Agnosia is a relatively rare neuropsychological syndrome defined in the classical literature as a failure of recognition. Agnosia is most often modality specific. Visual, auditory, and tactile agnosia have received the most attention and will be reviewed briefly in this chapter.

1. Visual agnosia : Lissaur divided the syndrome into two subtypes : "apperceptive" and "associative" visual agnosias. [12] In apperceptive visual agnosia, patients usually seem blind, in that they can not recognize objects, describe what they see, or even copy or match simple line drawings of objects. It usually occurs with bilateral occipital or parieto-occipital lesions. Associative visual agnosia is a more clearly defined agnosic syndrome. These patients also fail to recognize fictures and objects, but they can describe the elements of drawings, produce surprisingly accurate copies of drawings and pictures they can not name, and match drawings and pictures. Autopsy-studied cases of associative visual agnosia demonstrated bilateral occipital lesions.

2. Cortical Blindness (Anton's Syndrome) :

Total blindness, or loss of visual perception, occurs with bilateral occipital or parieto-occipital lesions destroying the primary visual cortex or optic radiations. Patients with new onset cortical blindness are often unaware that they can not see. These patients may attempt to walk and bump into objects. Anton attributed the lack of awareness to interruption of white matter pathways from the occipital cortex to other centers. Some residual vision of cortical blindness may be mediated by subcortical connections, such as those from the optic tracts to the midbrain.

3. Prosopagnosia : Prosopagnosia is a subtype of visual agnosia in which a specific recognition deficit exists for faces. The anatomical localization of prosopagnosia has been controversial. More recent studies involving autopsy or CT scans have demonstrated bilateral lesions in the occipital region. [6] The medial temporal areas are also involved. Prosopagnosia can also occur in the late course of dementias.

4. Balint's syndrome : The syndrome include optic ataxia, visual disorientation, and oculomotor apraxia. Optic ataxia refers to apparent incoordination of extremity movement under visual control. Visual disorientation or simultanagnosia refers to inability to catch whole impression of the pictures when the patients are shown detailed pictures. They describe only one small detail of a picture. Oculomotor apraxia refers to the patient's inability to direct gaze voluntarily in any direction from a fixation point. Bilateral parieto-occipital lesions may be associated with Balint's syndrome.

2. Auditory agnosia : Auditory agnosia are divided into three categories : a) cortical deafness, b) pure word deafness, c) auditory agnosia.

a. Cortical deafness : Profound hearing deficits are seen in patients with acquired lesions of both primary auditory areas, b. Pureword deafness: These patients have intact hearing for pure tones and nonverbal sound but cannot understand words. This

disconnection could be produced by either bilateral temporal lesions or a strategically placed left temporal lesion, c. Auditory agnosia : Those patiens fail to recognize both verbal and nonverbal sound reflecting bilateral temporal damage.

3. Tactile agnosia : The concept of tactile agnosia implies a failure of recognition in the tactile modality not explained by primary sensory loss or by aphasia or dementia. Tactile agnosia is the least clear and least understood agnosia syndrome. Lesions of the corpus callosum or dept white matter can produce such deficit. Astereognosis may be considered as an unilateral tactile agnosia.

Table I

Shows the Different Neurobehavioral Syndromes due to Left, Right and Bihemispheric Disease

1. Neurobehavioral syndromes due **to** left hemisphere disease:

   A. Aphasia
   B. Apraxia
   C. Alexia
   D. Verbal amnesia

2. Neurobehavioral syndromes due **to** right hemisphere disease :

   A. Visuo-spatial disburbances
   B. Neglect
   C. Right hemisphere and emotion
   D. Motor impersistence
   E. Nonverbal amnesia

3. Neurobehavioral syndromes due **to** bihemispheric disease :

   A. Amnestic syndrome
   B. Agnosias
   C. Special syndromes

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