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Review Article

Agnosia: Definition, clinical contexts, neurobiological profiles and clinical treatments

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Abstract

Starting from the general concept of Agnosia, the present work focuses on the clinical, neurobiological, and functional aspects of the morbid condition, suggesting a multidimensional treatment between rehabilitation exercises for lost skills and psychotherapy.

Contents of the manuscript

Agnosia (from the Greek *a-gnosis*, "not knowing") is a disturbance of perception characterized by the lack of recognition of objects, people, sounds, shapes, smells already known, in the absence of memory disturbances and the absence of system lesions elementary sensory. It can occur separately about each of the five senses and for each sense different types of agnosia can be found; in essence, the person suffering from agnosia can use a fork instead of a spoon thinking that they have chosen the spoon, or a shoe instead of a cup or a penknife instead of the pencil [1].

The first cognitive operational model on object recognition was developed by the German neurologist Lissauer, in 1890, who hypothesized that this recognition occurred on two consequential levels of analysis [2].

At the *first level* (perceptual level) the integration of elementary sensory data takes place in complex forms;

At the *second level* (associative) there is a comparison between what is perceived and the knowledge stored in memory.

This model, although still extremely valid today, other extremely valid models have been proposed, based on more in-depth theories regarding the various levels of stimulus processing, especially about visual perception. It often involves damage to the areas of the primary visual cortex and the associative areas via the what and via the where; not surprisingly, a deficit of the first level involves an apperceptive agnosia, while a deficit of the second level leads to associative agnosia. Therefore, starting from the sensory data, as a product of stimulation and receptor reactivity, through the five senses (sight, hearing, smell, touch, and taste), we arrive at perception, such as the elaboration of the elementary sensation that reaches the sense organ [2].

Thanks to the studies of Weber (*on the differential threshold or threshold of relevance of the perceived stimulus*) and Fechner (*on the sensation, directly proportional to the logarithm of the intensity of the stimulus*), we came to say that [2]:

1) The thesis that supported "sensation = perception" (naive realism) is incorrect, while the hypothesis that foresees the analytical difference (critical realism) is correct;

2) Only the stimuli to which the sense organ is sensitive are perceived;

3) The stimulus, to be registered by the sense organ, must be sufficiently intense, in an absolute sense.

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In the context of "*critical realism*" several theoretical approaches are distinguished [2].

1) An *associationist or atomistic approach* by Helmholtz (1878), which provided for a perceptive system made up of 2 systems that are relatively separate but communicating with each other: elementary sensations (I) and cognitive apperceptive layer (II);

2) *Gestalt approach*, which preferred to pay attention to form and representation. Therefore, several authors contributed:

a) For Metzger, the level of visual perception is not flat but three-dimensional;

b) For Rubin, the visual field is differentiated in the background and figure;

c) For Wertheimer, the perceptual field was organized by a series of rules: good shape (the perceived structure is always the simplest); proximity (the elements are grouped according to distances); similarity (tendency to group similar elements based on similarities); proximity (tendency to group similar elements based on close distance); closure (tendency to group similar elements based on known closed forms); continuity (all elements are perceived as belonging to a coherent whole); common destiny (if the elements are moving, those with a coherent movement are grouped); figure-background (all parts can be interpreted both as an object and as a background); pregnancy (in case the stimuli are ambiguous, the perception will be good based on the information taken from the retina).

3) The *cognitive approach*, which provided for the integration of the models:

a) Top-down, i.e. processing from top to bottom (guided by experience that influences perception);

b) Bottom-up, i.e. the processing from the bottom up (guided by the sensory data processed than in the cortical way). A typical example is Gibson's ecological approach, which provides for very specific assumptions: the stimulus is described not in terms of retinal projection but in terms of "optical structure" (ie image that reaches the retina); the stimulus (except pathological deficits) is perfect as it is and then it all depends on the subsequent interpretation; the set of information given by the context and movement of the observer is called "environmental optical set-up".

4) *Constructivist approach*, which has its foundation in the following assumption: "perception is an inferential process (ie based on hypotheses), given that the sensory information coming from the external environment is ambiguous and incomplete, to reach perception it is necessary to the intervention of top-down processes ". Therefore, perception: it is an inferential and active process; it is the final process of the interaction between stimulus (from below) and experience (from above); it is a process that is influenced by various external factors (example, visual disturbances, psychiatric disorders, wrong perception, illusion, hallucinations, delusions, suggestion, impossibility of perception due to the sense organ). Among the major exponents we mention:

a) Gregory: Starting from Gibson, he says that the starting point is the external stimulus but then we activate the best possible interpretation to explain the complex object);

b) Necker: Between two possible interpretations, one will always prevail;

c) Allport: Proposed the "perceptual set", that is the idea that the field is influenced by subjective motivations, emotions, experiences and expectations, reorganized according to two cognitive operations that we will see later: "generalization" and "categorization".

5) *Synthetic approach*, or the schools of thought adhering to neuroscience, which attempt to overcome the top-down/ bottom-up relationship, effectively integrating two models. Among the major exponents we mention:

a) Bruner: Perception depends on one's needs, expectations, moods, subjective values, emotional meaning, and personality characteristics (New Look School).

b) Neisser: The brain is a computer and perception is nothing but an analysis by synthesis, the result of a three-stage sequence: I) the selection of the stimulus through an automatic pre-attentional (bottom-up) process; II) the voluntary shift of attention on the stimulus (top-down); III) the final mental representation.

c) Marr: Perception can be investigated on at least 3 levels (computational theory): I) computational level (the goal); II) algorithmic level (the means used); III) procedural level (the how). Marr's approach is strongly bottom-up (as it focuses on sensory processing) but includes the intervention of "top-down (ie information previously learned from the world)" factors: << the chair must have four legs to be able to stand. So our knowledge of the world (top-down) acts on sensory input (bottom-up), reaching a perceptual synthesis >>. The analysis of the visual sensory input proceeds through four specific stages: a) description of the gray levels; b) geometric primitive primary sketch; c) two-dimensional sketch and ½ (example, depth); d) 3D representation (three dimensions). However, this model is strongly criticized because it does not take into account an adequate explanation of how the factors at playwork and there are no functional tests outside the laboratory context.

Regarding the human ability to recognize faces and objects: the ability to recognize faces is a typical basic characteristic that has a high degree of social relevance and is vital for newborn babies who at thirty minutes of life seem to already show a preference for faces. The action of recognizing faces is something we can do quickly and automatically, it is a function that is acquired early during the development phase and that does not need to be taught. Face processing takes into account a large number of perceptual and cognitive processes. Two scholars, Bruce and Young, in 1986, proposed a theoretical model for face recognition. This model involves a sequential and hierarchical organization of different degrees of processing. According to the two authors, face recognition is based on an abstract unit that contains different types of structural information of each face that is present in memory.

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At a lower level of this processing, there is a perceptual analysis of what are the facial features that are done by a structural coding component and the result of which is stored in a face recognition unit, called Face Recognition Unit. Bruce and Young's model has become classic for research on the perception of faces. It provides that from a face it is possible to obtain different types of information which are then processed in different cognitive components and in the subsequent processing stages which are [3].

a) Structural encoding: In this stage, the structural aspects of a face are analyzed, so that it can be distinguished from others. It is a 3D processing of the face, automatic and unaffected by top-down processes.

b) Face recognition Unit: Represents each of the facial recognition units and contains the structural information on the faces known to the observer, the information that allows a face to be recognized compared to other faces. Here the familiarity of the faces is described, the descriptions of the people we know.

c) Person identity nodes: Concern the identification of the person, for example, the profession or his interests.

d) Name generation: Concerns the recovery of a person's name.

Bruce and Young argued that the difference in processing between familiar faces was not because there are structural codes stored for the faces that are known and that are processed through frequent exposure to the stimulus. In the original Bruce and Young model, there are no recognition units for unfamiliar faces. A model such as that of Bruce and Young focuses mainly on cognitive processes as regards face recognition, while more recent models have included affective aspects. According to these models, there are two ways, a cognitive one that analyzes the identity of the face and allows us to access the names of the people we know and a second way involved in the production of affective responses in front of faces familiar to us. The cognitive pathway is connected to the identity nodes of the person and activating the semantic information supports the recovery of the name. Any anomaly in this way could, therefore, cause a deficit in recognizing the faces that would explain the prosopagnosia, while a deficit in an affective way could cause a loss of skin conductance responses, in a different way for family and non-family stimuli. Patients with prosopagnosia, although unable to recognize familiar faces, are able, however, to recognize familiar objects. This could happen because the differentiation between one face and another must be more precise and detailed than, for example, that there can be between classes of objects or because there are specific mechanisms used only for the recognition of faces and which do not concern the recognition of objects. If the processing of faces concerned specific mechanisms, the existence of distinct brain regions associated with the recognition of faces and objects should be considered realistic. However, many studies conducted with PET and fMRI have revealed conflicting results with such a hypothesis [4].

The recognition of the objects, therefore, implies the comparison between the information that derives from the visual stimulus and that which is recorded in the memory. Both proponents of theories of shapes and those of theories of characteristics agree on this. The theory of shapes is based on the fact that a miniature copy exists, called a template that is stored in long-term memory and which corresponds to each visual configuration that we know. The simpler the more similar to the stimulus presented is the easier the configuration is recognized. This theory, however, is not very realistic because there can be a huge number of visual stimuli that can combine with the same shape. For the theory of characteristics, a given configuration consists of a series of specific attributes, called, precisely, characteristics. For example, a face has various characteristics: the eyes, the mouth, the nose. These characteristics are compared with the information that is stored in the memory. In 1982, Marr proposed a computational theory concerning the processes involved in object recognition. According to Marr, there are a whole series of representations that provide us with detailed information on the visual environment and are of three types. The theories concerning the recognition of objects can be divided between those that depend on the point of view and those that are independent of them. For the latter, the ability to recognize an object is not influenced by the observer's point of view, for the former, however, the observer's point of view may be able to change the accuracy and time that we use or not in recognizing a certain object. We have seen how both theories can be valid, since there are cases in which mechanisms are used in the recognition of objects that are independent from the observer's point of view and others, however, in which the opposite occurs. The mechanisms that do not depend on the observer's point of view are more important when it comes to distinguishing between categories of objects, while those that depend on the point of view are more important when it comes to grasping the differences within the same category [3,4].

Concerning the clinical classification, the best thesis recognizes the following forms of agnosis [5,6,7-9].

Appreciative agnosia: We speak of apperceptive agnosia when the subject, in the absence of sensory deficit, is unable to compose the stimulus data and integrate them into a structured perceptual unit. A patient with apperceptive agnosia in the visual modality is unable to perform a drawing on a copy, to accurately describe it in its details and to distinguish it from visually similar objects. Consequently, the comparison with the mental representations of known stimuli also fails, and therefore the recognition of the stimulus does not take place. Humphreys and Riddoch, about Marr's model of perceptual processes, classify three main forms of perceptive agnosia:

a) Agnosia for shape: The patient correctly analyzes the individual sensory characteristics of the stimulus, but is unable to derive the external configuration of the object. If tested, it is unable to match identical geometric shapes or distinguish different shapes, and is unable to copy simple shapes.

b) Integrative agnosia: The patient fails to integrate the individual characteristics into a unified global structure. For

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example, a figure with many details will not be recognized, while a figure with few details will not be recognized. The patient can perceive the parts of a dog (legs, ears, tail) but does not integrate them to represent the shape of the dog, or he does it with great difficulty.

c) Transformational agnosia: The patient cannot transform the global structure of the object to compare it with a prototypical representation available in the pre-semantic warehouse. For example, it is unable to recognize an object if rotated, turned upside down, varied in size, or viewed from a different angle.

Examples of these particular forms of agnosia may be the "anosognosia", the inability to recognize one's pathology or deficit, the "autotopoagnosia", the inability to identify and direct the different parts of the body in space and the lack of recognition of the own body and parts of it and the "unilateral spatial negligence", the difficulty in exploring the contralateral space to the lesion of the inferior parietal lobule or the subcortical areas of the Talamo and Putamen.

Associative agnosia: Associative agnosia occurs when a patient, whose perceptual analysis is intact, is unable to compare the structured perceptual representation of a stimulus with the knowledge present in the semantic warehouse (relating to known stimuli) and therefore to activate the relative knowledge to the object (its name, correct use, etc); therefore the deficit is only about the semantic categorization of an object. For example, the patient may be able to visually recognize a fork as a known object ("intact perceptual analysis"), but cannot say what it is used for, on what occasions it is used and what it is called, although this knowledge is present, as demonstrated by the fact that if asked verbally to describe a fork he can correctly say what it is and how to use it. So the deficit is in access to the semantic warehouse on visual stimulation, which is why Humphreys and Riddoch call this semantic access agnosia disorder. Associative agnosia is generally associated with sinister occipitotemporal lesions.

Sensory agnosia: They are all typologies that concern a particular sense where its function is impaired, failing to recognize what it sees, feels, tastes, or touches, the most particular of these forms is that which concerns touch. In this case, it is caused by damage to the parietal-temporal cortex, varying in severity, where the worst form is given by left cerebral infarcts. Among the forms of "visual agnosia" can be mentioned: "prosopagnosia", agnosia for faces, "akinetopsia", agnosia for movement, and "achromatopsia", agnosia for colors. Among the "auditory agnoses": agnosia for environmental sounds, agnosia for the human voice, and agnosia for musical arias. Bilateral lesion of the temporal lobes is found in all three cases in particular. Among the "tactile agnosias" or "astereognosias": the "amorphognosy", which concerns the shape and size of the objects, the "ailognosia", which concerns the weight and the material and thermal characteristics of the objects, the "asymbolism" or " tactile agnosia ", which concerns the meaning of objects and" tactile agnosia ", which consists in the inability to recognize one's hands.

From an etiopathological point of view, agnosia is caused by damage to the parietal, temporal, or occipital lobe of the brain. These areas store memories of the use and importance of familiar objects, sight and sounds, and integrate memory with perception and identification. Often, agnosia suddenly appears after a head injury or stroke. Other causes of agnosia include brain tumors, brain abscesses (pockets of pus), and disorders that cause progressive areas of the brain to degenerate, such as Alzheimer's disease [6].

The symptoms of agnosia therefore vary according to the damaged lobe [5].

a) "Parietal lobe": people have difficulty identifying a familiar object (such as keys or a safety pin) positioned in the hand on the side of the body opposite to the damage (somatosensory agnosia). However, when they look at this object they immediately recognize it and can identify it. Some subjects with damage to a parietal lobe insist that everything is fine or ignore the problem, even if one side of the body is paralyzed (anosognosia);

b) "Occipital lobe": people are unable to recognize familiar objects, such as a spoon or pencil, even if they can see them. This pathology is called visual agnosia. They may not recognize familiar faces (prosopagnosia);

c) "Temporal lobe": people may not be able to recognize sounds, even if they can hear them. This pathology is called auditory agnosia;

d) "Occipitotemporal lobe": people may not recognize familiar places (environmental agnosia) and suffer from color blindness.

The patient suffering from agnosia is diagnosed after an anamnestic evaluation and the use of diagnostic brain imaging equipment. The physical examination is performed to highlight primary deficits in individual sensory modalities or communication skills that may interfere with neurobiological testing. For example, if there is damage to superficial tactile sensitivity, patients may not perceive an object, even when cortical function is intact; in addition, the presence of possible aphasia may interfere with patient expression. Neuropsychological examination may also help to identify more nuanced agnosias. Neurological examinations (CT or MRI with or without hagiographic sequences) are necessary to characterize a lesion of the central nervous system (e.g. heart attack, bleeding, mass) and to assess the presence of atrophy leading to degenerative disease [3].

To complete the clinical picture, the patient undergoes specific neurocognitive tests [4], which aim to assess individual abilities, and specific personality tests, which will provide detailed information on his mental health status; for example, the diagnosis of agnosia may exacerbate any anxiety [10,11] and mood disorders suffered by the patient as a result of the traumatic event [12,13], up to panic disorder [14], major depressive disorder [15], obsessive disorder [16,17], or even encroaching on psychotic symptoms where the plane of reality is wholly or partly compromised [18]. If the aetiology of agnosia

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derives from a degenerative neuropathological condition [19-21], the risk of suicide increases compared to the average [22].

The prognosis will obviously depend on the type, size and position of the lesions, the degree of impairment, the age of the patient and the targeted effectiveness of drug therapy, rehabilitation [23] and speech therapy and psychotherapy [24].

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