BRAIN, IMAGING AND IMAGINATION

HOW THE BRAIN REPRESENTS THE WORLD

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IMAGING BRAIN ANATOMY
SUPRAMODALITY
VISUAL IMAGERY
CONCEPTUAL REPRESENTATION
AGGRESSIVITY

The present work aims to describe the main results obtained from the neuroimaging studies on the study of those cognitive processes related to imaging and imagination. A brief excursus on the development of modern neuroimaging techniques presents the methodological background of the many studies. The relationship between sight, blindness and conceptual representation is explored. Research has shown that the ventro-temporal cortex is responsible for recognizing the surrounding environment, to distinguish an object from a face and, in general, objects' categorization. This area is responsible of imagery in both sighted and blind people, being its morpho-functional organization independent of the visual experience. It follows that a very precise classification of all categories of objects could be obtained in the human brain, and it is supported by a distributed cortical representation independent from the sensorial modality. The last part of the paper presents a series of studies, in which the study of imagery was related to aggressivity. The prefrontal cortex is deactivated when an individual imagines himself becoming aggressive, being this effect more relevant in females than in males. As a conclusion, the neuroscientific approach produced important results in the definition of what imagery is, and showed its relevance to the study of how mind and brain work.

The interest in brain morphology is old, so as the interest about how the conscious life, mental activity and cognitive functions could emerge from the brain structures. Andrea Vesalio, known as the founder of modern anatomy, wrote in the famous text "*De Humanis corporis Fabrica*", in 1543: "*Non nego che i ventricoli elaborino lo spirito animale, ma sostengo che questo non spiega nulla sulla sede cerebrale delle facoltà più elevate dello spirito. (...) Non sono in grado di comprendere come il cervello possa esercitare le sue funzioni*". (*)

Before the development of modern methods for the morphological and functional exploration of the central nervous system, in the mid-eighties of the last century, the studies on the brain focused on the observation of individuals, who had suffered from injuries. The first descriptions of serious personality and behavioral disorders, due to a brain injury, appeared in ancient times. One should think of the famous case of Phineas Gage described by the doctor John Martin Harlow in 1848 (Harlow, 1848). Gage served as a foreman in the construction of the railway line in Windsor County, Vermont. One morning he was victim of an accident at work, following the accidental triggering of an explosive charge. Gage was struck by an iron bar that penetrated the left cheek, pierced the skull, and came out of the frontal top. The Gage case has remained in the history of neuroscience, neurology, and psychiatry, not only because Gage was miraculously able to survive, but also because his character and personality changed radically, so that acquaintances concluded that "Phineas was no longer himself".

It was soon realized that some fundamental functions were lacking in patients, who had suffered from lesions in the frontal lobes, like that of Gage. In fact, such lesions produce an unusual range of emotional, cognitive and behavioral changes. With the development of modern methods for morphological and functional in vivo brain exploration (such as positron emission tomography [PET], structural magnetic resonance [MRI] and functional magnetic resonance [fMRI]), it was possible to study the fine anatomical and functional architecture underlying the several cognitive activities and the most complex and elusive mental functions. For example, emotional experience, behavioral control, abstract thinking, moral judgment, planning skills, programming, the distinction between good and evil, respect for norms, and social conventions (Koechlin et al., 2000; Nichelli et al., 1994; Pietrini, 2003; Raichle, 1994).

In their entirety, the results of neuroscientific research show how these sophisticated mental functions can be linked to the activity of precise brain structures, mainly located in the frontal lobe. By comparing the development and organization of the cerebral cortex in the human brain and brains of animals phylogenetically close to man (such as monkeys), we can see how the prefrontal cortex developed much more in the human brain.

Therefore, through the study the cerebral correlates of certain functions (such as abstract thought, moral judgment, the conceptual representation of the external world, and so on), we understand that the human being is the best, if not the only, animal model to be considered. In ancient Greek language, the verb "to know" οἶδα (pronounced "oida") was the perfect tense of a verb that indicated the act of seeing (cf. ὁράω, pronounced "orao"), and meant "I saw, and therefore I know". It also indicates that knowledge could not be independent from the visual experience. Even today, the relevance of sight is indicated by the frequent use of terms based on visual verbs: "Can you see my point?", "I see what you mean", "*Vedere la vita in rosa*", "*Stravedere per qualcuno*", "*Arrivederci*", and so on. (**)

From a neurophysiological point of view, the relevance of sight is in agreement with the finding that the cerebral cortex related to visual functions represents almost a third of the entire surface of the cerebral cortex.

These first considerations give rise to a spontaneous series of questions, not only from a neuroscientific point of view. How can people with congenital blindness represent a world they have never seen? How do they use brain structures dedicated to vision in the absence of sight? And, again, to what extent is sight really necessary for the brain to develop its wonderful morphological and functional architecture? Finally, what can we learn from the study of the brain of blind individuals, about how the brain develops and functions in physiological conditions? Thanks to modern methods of in vivo exploration of brain functioning, we can look for the answer to these questions. In particular, through functional magnetic resonance imaging (fMRI), a non-invasive biomedical imagining technique, we can observe the brain at work and obtain a map of functionally informative brain areas.

Through functional magnetic resonance experiments, we were able to outline the functional topography of the visual pathways in humans. After that the stimulus reaches the primary visual cortex, it is split into two parts. One part proceeds on the ventral way, also called the "what pathway", though which we recognize the external world. The other part proceeds on the dorsal way, also called the "where pathway", which is the one allowing us to place objects in space (Haxby et al., 1994). Consequently, if we want to move in the surrounding world, these two areas of the brain must necessarily talk intensely with each other, to be able to recognize the objects around us and place them in the space. In some diseases, e.g., the Alzheimer's disease, the ability of different areas of the cerebral cortex to communicate with each other is lost even before that focal alterations (that is, to parts of the cortex) occur. This is also known as an alteration of functional connectivity (Grady et al., 2001; Pietrini et al., 1993; Pietrini et al, 2009a).

The ventro-temporal cortex (a small part of the cerebral cortex formed by the ventral part of the temporal lobe) allows us to recognize everything that surrounds us, and to distinguish an object from a face as well as different categories of objects between them. This topic has always fascinated the world of neuroscience, psychology, and cognitive sciences.

In a study published in 2001 (Haxby et al., 2001), we used three Tesla magnetic resonance imaging to understand the neural correlates for recognizing different categories of objects. We examined brain activity in response to visual recognition of objects belonging to different categories: faces, animals, artificial tools, chairs, places, and everyday objects.

The results demonstrate that the brain response is distributed throughout the entire ventro-temporal cortex, in a largely overlapping manner for all the categories examined. However, the pattern of brain response appears to be highly specific for each category, so much that we can predict, with great accuracy, what the subject is looking at. In other words, there is a very strong correlation in the response within the same category. That is, the response that the brain provides when we look at a face is significantly correlated within the category of faces, but it is not correlated with the response obtained with brain activity related to other categories. Therefore, we can state the existence of a categorical specificity.

The study by Haxby and colleagues (2001) led to the development of a new model called Object Form Topography. According to this model, the ventral-temporal cerebral cortex does not respond in an all-or-nothing way to certain categories of objects. Rather, it can produce an infinite series of specific patterns of neuronal response. As mentioned above, these patterns are particularly specific and can predict what the individual is looking at. To our knowledge, this is the first study of Brain Reading, addressed to decode a neural signal in such a specific way to be only referable to a specific mental activity.

At this point, a question arises about the conceptual representation: is the functional organization of the cortex only visual or does it represent a more abstract representation of the external world? To test this hypothesis, we conducted a series of functional magnetic resonance studies, in which subjects were blindfolded and were required to recognize objects of different categories, though the tactile (not visual) modality.

Subjects had to perceive objects with their own hands, for example, by touching casts of human faces or other types of objects, such as shoes or bottles. The tactile exploration showed a strong activation, not only of the somatosensory cortex, but also of the ventro-temporal visual cortex, congruently with what happens for visual recogni-

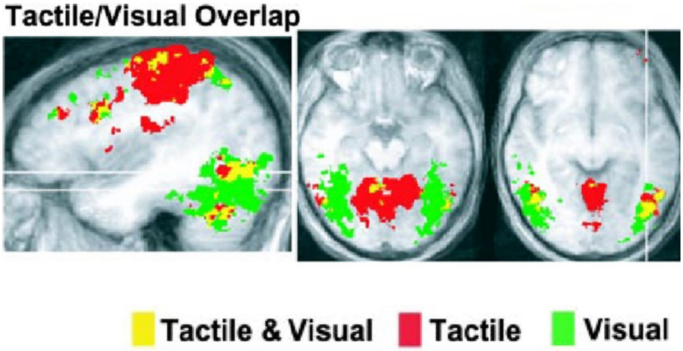


Fig. 1 The figure shows the areas of the ventral-temporal cortex activated in response to the visual perception (in green) or tactile (in red) of different categories of objects. The areas of the cortex that are activated in response to both visual and tactile perception are reported in yellow (from Pietrini et al., PNAS, 2004, modified).

tion. If we superimpose and compare areas activated during visual recognition and those during tactile recognition (Figure 1), we realize that there are areas of the ventro-temporal visual cortex that are activated in both cases.

Several studies show that there is not big difference for the brain between seeing something concretely or imagining to seeing it (Pearson et al., 2015). It follows that, if we touch an object and explore it with our touch, we immediately evoke the visual image of the object that we are touching: this process is called visual imagery (Cattaneo et al., 2008).

How can we, therefore, exclude that this activation in the ventral-temporal cortex during tactile exploration is not simply due to visual imagery? To provide an answer to this question, we asked people with congenital blindness - who have never seen the world around them and therefore do not have a conceptual representation coming from a visual experience - to recognize objects through tactile exploration.

As shown in Figure 2, the visual cortex of these subjects is activated in the same way and with the same categorical specificity as in the sighted persons, when they see or touch the same object. Given that the congenital blind person has no visual experience and, therefore, no visual imagery, we can reasonably assume that the ventro-temporal cortical activation, occurring during the tactile recognition of different categories of objects, cannot be attributed merely to visual imagery (Pietrini et al., 2004).Therefore, the morpho-functional organization of the ventro-temporal cortex is independent of the visual experience. This property has been defined as supramodality, which is the ability to process perceptual information independently from a specific sensory modality (Pietrini et al., 2009b; Ricciardi et al., 2014). Thus, from perception, we move to what could be defined as a conceptual representation. How are concepts related to our surrounding space coded in the brain? We run an experiment in collaboration with scientists on neurolinguistics of the University of Pisa, in which sighted as well as blind from birth individuals were asked to describe the characteristics of different objects. Objects belonged to different categories as mammals, birds, fruits, vegetables, tools, vehicles, natural places, and artificial places.Through a verbal description, it is possible to reconstruct some maps of conceptual representation that group objects together using a property-generation task. These maps are called "behavioral representational similarity maps". The experiment required that sighted subjects read the name of the referenced object (Verbal Visual Form) or see the image projected (Pictorial Visual Form), or even listen to the name of the referenced object (Verbal Auditory Form). In a time frame of seven seconds, sighted subjects verbally described what they saw or listened to (for example: pineapple: it is a fruit, it is sweet, etc.; cat: is a mammal, meows, has a tail, etc.; bar: it's a place where you get together, they serve coffee; and so on). Obviously, only the acoustic mode was used for blind subjects, by listening to the name of the referenced object.

These experiments highlighted the link between the spatial representation of the different categories of objects - obtained through the verbalization of the categories - and the possibility of reconstructing the conceptual maps of the objects - based on the patterns of cerebral activation. If we then analyze the whole brain, instead of the visual cortex only, both the correlation and a notable improvement in the segregation between the different objects occurs. Then, a very precise classification of all categories of objects (separated from each other) could be obtained when all the areas that cooperate to this classification are included in the analysis.

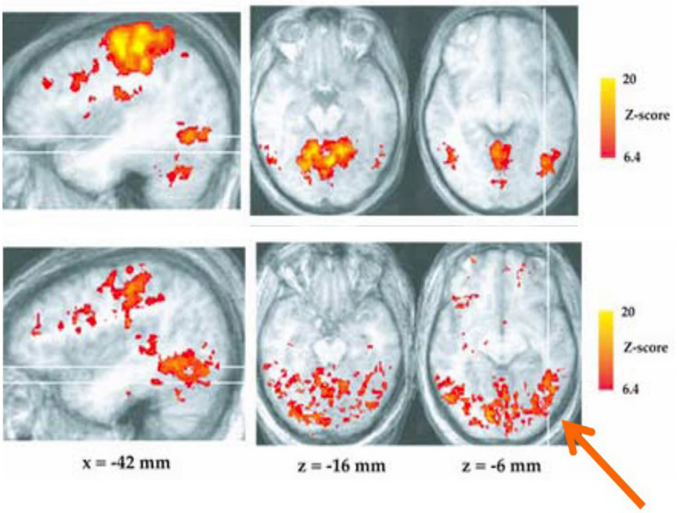


Fig. 2 The figure shows the areas of the ventral-temporal cortex activated in response to tactile perception in visually impaired (above) and blind subjects from birth (below). The arrow indicates the areas of the "visual" ventral-temporal cortex activated by the tactile perception in the blind subjects from birth (from Pietrini et al., PNAS, 2004, modified).

This shows that the conceptual representation of an object of a given category in the human brain is supported by a distributed cortical representation independent from the sensorial modality, which does not differ significantly between those who had a visual experience and those who had not. This representation is also independent from the visual experience and the sensory modality used to collect the information (Handjaras et al, 2016, 2017).

The existence of functional cortical organization, more abstract than what was expected, shows how the brain is programmed to develop independently from the visual experience. It is not yet known how much the brain is genetically programmed and how much it depends on stimuli from the environment, although it is highly probable that the brain needs *some* sensorial experience, anyway. Such an organization allows individuals who are blind from birth to acquire knowledge, to create mental representations, to learn from others and to actually interact with an external world, which they have never seen (Ricciardi and Pietrini, 2011). Thus, the brain can develop its anatomical and functional architecture independently from the visual experience. This can be considered a clear advantage also from an evolutionary point of view. After the discussion about perception, and after the definition of conceptual representation, it is now time to present the concept of *Imagery*.

IMAGES, IMAGERY AND IMAGINATION. CAN THE BRAIN IMAGINE BECOMING AGGRESSIVE?

Using the recent methodologies of morphological and functional exploration of the central nervous system, we can wonder, for example, what happens in our brain when we make a decision, when we interact with others, when we respond to the outside world, or when we become aggressive. From a neurobiological and evolutionary point of view, aggression is the implementation of a behavioral response aimed at benefiting the individual.

A few years ago, we investigated what happens in the brains of healthy young people, who do not have behavioral disorders or a history of violence, when they are asked to imagine themselves in a situation where they must express aggression. Healthy individuals, subjected to Positron Emission Tomography (PET), with marked water to measure changes in cerebral blood flow [1], had to imagine being in a confined environment (an elevator) with their mother, along with two strangers. On a certain moment, one of the two strangers assaulted the subject's mother, in different scenarios. The subjects had to react thinking to attack this person and beat her, even to the point of killing her (Pietrini et al., 2000). The results of the study showed how, when the individual imagines himself becoming aggressive, his prefrontal cortex is functionally inhibited, in a sort of functional shutdown, that is, deactivated with respect to emotionally neutral conditions. Furthermore, this deactivation was much more significant in females than in males, probably because imagining physical violence is an even more unnatural act for a female than it is for a male. This is congruent to the finding that the scores of aptitude for violence are significantly greater in males than in females (Figure 3).

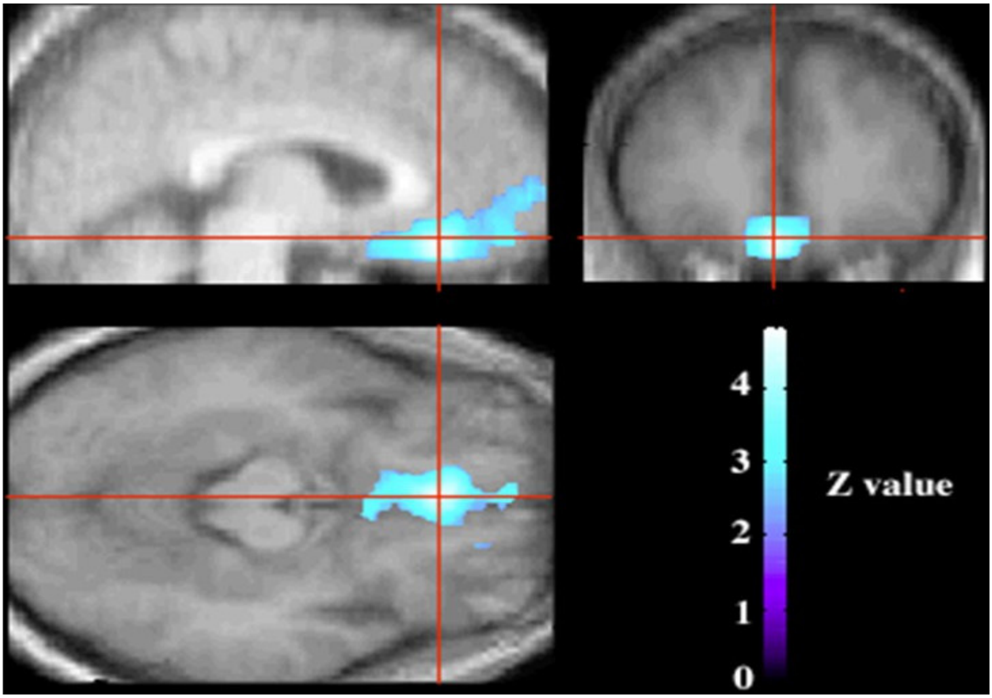
These in vivo functional data, in agreement with the evidence of clinical literature, demonstrate the importance of the prefrontal cortex in the modulation of aggressive behavior and, more generally, of social behavior and impulse control. The definition of functional neuroanatomy, which underlies the control of behavior, opens the perspective to the study of the brain correlates of criminal behavior. How much is the criminal really free? Or, is that person a criminal because he or she cannot be different from what he or she is (as also summarized in the word game "Bad or Mad" in Anglo-Saxon literature)?

More than a hundred years ago, the English psychiatrist Henry Maudsley (1835-1918), describing criminal psychopaths, wrote: "As there are people who cannot distinguish certain colors by having what is called color blindness, and others who have no ear for music cannot distinguish one musical tone from another, in the same way, there are some that are congenitally lacking of any moral sense". This is a statement made many years before the advent of any methodology for the scientific investigation of the central nervous system. With the modern methods available, we could nowadays compare healthy non-psychopathic subjects with psychopathic criminals, and we are able to detect the presence of selective anatomical brain differences between the two groups of subjects (Figure 4).

In fact, there is a neuronal reduction that does not concern the whole brain but is only concentrated in the prefrontal cortex and in some areas of the limbic system. It is well known that the prefrontal cortex is important to the control of aggressive behavior and the limbic system to emotional-affective regulation (Ermer et al., 2012). This difference remains statistically significant even when all the possible confounding factors have been taken into consideration, for example: the level of education, psychiatric history, head injuries, alcohol, drug abuse, and so on. Hence, the psychopathic criminals have a prefrontal cortex with significantly reduced thickness, nerve cells population (over 20% fewer neurons) with respect to control subjects, and with an altered functional connectivity (Ermer et al., 2012; Anderson & Kiehl, 2012; Ly et al., 2012). However, this observation does not tell us whether a) these individuals behave this way because they are criminals, or b) they are criminals because they are like that. In other words, we are faced with the famous egg-chicken dilemma. To understand what is the cause and what is the effect, longitudinal studies are needed on large groups of subjects, starting from the stages of early adolescence. It would be even better to combine these studies with studies on genetic factors that modulate a) vulnerability to the environment in childhood and b) the risk of developing antisocial behavior in adults (Byrd & Manuck, 2014; Caspi et al., 2002; Iofrida et al., 2014 ; Pietrini & Rota, 2013; Rota et al., 2014).

As a conclusion, the long journey in the Imaging Brain Anatomy has begun many years ago with the anatomical studies, in which Italy has been at the forefront. Then, it continued with the possibility to study *in vivo* neuroanatomy with high-resolution, achieving the step of overlapping structure

Fig. 3 The figure shows the reduction in work (in blue) in the areas of the prefrontal cortex of healthy subjects during the expression of aggressive behavior at the imaginary level (from Pietrini et al., PNAS, 2004, modified)



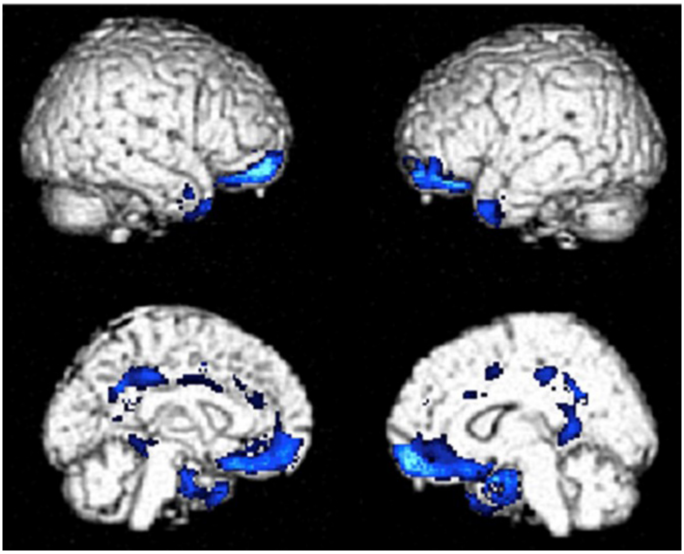


Fig. 4 The figure shows the areas of the cerebral cortex with a significant reduction in neuronal density (in blue) in a group of psychopathic criminals concerning healthy control subjects (from Ermer et al., 2012, modified).

and function. Nowadays, it is possible to examine the brain in action while we perceive a figure, represent its meaning, plan a strategy, decide between good and evil. This is a fascinating journey into the brain, in search of the mind. Still, in the hope, which we all look for, of being able to find the crux of the matter about the complexity of the phenomena occurring in our brain (Pietrini, 2003).

NOTE

1 Cerebral blood flow is an indicator of brain activity: it increases where brain activity increases and decreases where brain activity decreases.

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