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**Review article**/Artigo de revisão/Artículo de revisión

# THE USEFUL INTERACTION BETWEEN FUNCTIONAL MAGNETIC RESONANCE IMAGING AND NEUROPSYCHOLOGY

## *A RELEVANTE INTERAÇÃO ENTRE RESSONÂNCIA MAGNÉTICA FUNCIONAL E NEUROPSICOLOGIA*

## *LA RELEVANTE INTERACCIÓN ENTRE RESONANCIA MAGNÉTICA FUNCIONAL Y NEUROPSICOLOGÍA*

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### ABSTRACT

In this paper, we aimed to elaborate a brief review about the early studies in functional magnetic resonance imaging (fMRI) associated to cognitive tasks, going over the most important researchers in the area, from William James to Seiji Ogawa. Moreover, we discuss studies that used cognitive tasks and fMRI in diseases such as epilepsy, autism, schizophrenia, multiple sclerosis, Parkinson's disease and dementia, in order to demonstrate the current and important interaction between neuropsychology and fMRI. From this review, we concluded that neuropsychology, a field of neuroscience used for diagnosing cognitive impairments, can be combined to technologies such as fMRI, producing extremely useful results for experimental and especially clinical contexts.

**Keywords:** Magnetic Resonance Imaging; Neuropsychology; Cognition.

### RESUMO

*O objetivo deste artigo foi fazer uma breve revisão acerca de como tiveram início os estudos em imagem de ressonância magnética funcional (RMf) associada a tarefas cognitivas, passando pelos principais pesquisadores na área, desde William James até Seiji Ogawa. Além disso, se relata que foi utilizado RMf e tarefas cognitivas em doenças como epilepsia, autismo, esquizofrenia, esclerose múltipla, doença de Parkinson e demência, a fim de demonstrar a atual e importante interação entre neuropsicologia e RMf. A partir deste estudo, concluímos que a neuropsicologia, uma área da neurociência bastante utilizada para o diagnóstico de prejuízos cognitivos, pode ser combinada a tecnologias como RMf e produzir resultados de extrema utilidade experimental e principalmente clínica.*

***Descritores:*** *Imagem por Ressonância Magnética; Neuropsicologia; Cognição.*

### RESUMEN

*El objetivo de este artículo fue el de hacer una breve revisión acerca de cómo tuvieron inicio los estudios en imagen de resonancia magnética funcional (RMf) asociada a tareas cognitivas, pasando por los principales investigadores en el área, desde William James hasta Seiji Ogawa. Además, se relata que fue utilizada RMf y tareas cognitivas en enfermedades como epilepsia, autismo, esquizofrenia, esclerosis múltiple, enfermedad de Parkinson y demencia, a fin de demostrar la actual e importante interacción entre neuropsicología y RMf. A partir de este estudio, concluimos que la neuropsicología, un área de la neurociencia bastante utilizada para el diagnóstico de deterioro cognitivo, puede ser combinada a tecnologías como RMf y producir resultados de extrema utilidad experimental y principalmente clínica.*

***Descriptores:*** *Imagen por Resonancia Magnética; Neuropsicología; Cognición.*

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Neuropsychology started as a field of neuroscience since the experimental simulation of behavior about 30 years ago. It was the only non-invasive method to observe the relationship between cognitive process and brain function.

However, nowadays neuropsychology is not alone anymore as an inferential process to the understanding of the structure-function correlation. There is the possibility to join this science with high technology techniques such as functional magnetic resonance imaging (fMRI) to observe the activation of cortical areas associated to motor, sensorial, emotion and cognitive functions.

Therefore, from the integration between both, it is possible to detect structure or functional lesions with a high spatial precision not just limited to provide clues of the localization from the impaired performance.

Then, how do that integration started? In this paper we will review some aspects from the beginning of the functional imaging and the importance of neuropsychology associated with fMRI and the experimental and clinical use in some neurological disorders.

## A brief review

Starting from Willian James in 1890 (Principles of Psychology)[1] and Angelo Mosso (1881)[2] we can find notes mentioning change blood- flow during cerebral activity, as well as Paul Broca (1979)[3] who was interested in circulatory changes associated with mental activity, because of alterations in brain temperature. He studied the effect of several mental activities, mainly language, measuring the temperature of the scalp of medical students. At the same time, Roy and Sherington (1890)[4] suggested a relationship between circulation and metabolism.

Nevertheless, Seymor Kety (1960)[5] and Lou Sokoloff (1977)[6] were the researchers who developed quantitative methods to measure the whole-brain-flow and metabolic in humans providing the first evidences that quantitative changes in blood-flow is directly related with brain function. Meanwhile, Neils Lassen (1963)[7] and David Ingvar (1965)[8] used scintillation detectors by a helmet and concluded that brain blood flow changes regionally in normal human during task performance.

A really important study by Ray Cooper et al. (1975)[9] registered the availability of oxygen in the human cortex in patients who would be undergone to epilepsy surgery performing motor and cognitive tasks.

Although there were many findings, the interest related to brain function and brain blood-flow was almost abandoned, for two reasons: first, there were no sophisticated tools to base these investigations and second, due the erroneous findings of Leonard Hill[10] who concluded that there was no correlation between brain functioning and cerebral circulation.

The interest came back, gradually, in 1928 when John Fulton[11] studied the visual attention to objects in the environment associated with blood-flow in the visual cortices. These conclusions were useful to the development of the computed tomography X-ray more than 40 years later by Godfrey Hounsfield.[12]

The computed tomography X-ray was a technique based on Alan Cormack (1963)[13] principles. Thereafter, researchers started a study using positron emission tomography (PET), in which they could create autoradiogram *in vivo* of brain functions to measure blood-flow and glucose metabolism. It was the first time that this technique was used in humans.

They also validated techniques for oxygen consumption showing that PET could provide precise measurements of cerebral function in humans. It became a required technique for being fast measuring (1min) using a short half-life (123seg) radiopharmaceutical ($H_2{}^5O$) enabling that the same person could undergo this process more than once.

The first studies using PET in humans performing cognitive tasks started in 1980 and encompassed cognitivist psychologists that were interested in understanding the human behavior by means of theory of information processing. This group got power when neuroscientists and scientists interested in imaging joined them and started researches related to strategies for functional mapping of neuronal activity, based on the thoughts' measurements associated to a simple logic based on the Dander's concept (1969).[14]

Finally, the magnetic resonance imaging came up bringing the fMRI to the scene when Fox and colleagues (1986, 1988)[15,16] reported that during changes in the neuronal activity there are local changes in the amount of oxygen consumption in the tissue.

These findings were associated with previous studies of Pauling and Coryell (1936)[17] and posteriorly described by Ogawa et al. (1990)[18,19] who provided evidences that changes in the blood oxygenation, *in vivo* could be detected using fMRI from the called T*2 (T-two-star). From this moment, the term BOLD (blood-oxygen-level-dependent) contrast became known.

So, Ogawa et al., in 1992[20], were encouraged to study human volunteers demonstrating the occurrence of intrinsic signal change in gradient-echo MRI at high-magnetic fields produced by visual stimulation which, clearly, produced activation in the occiptal cortices.

They suggested that T*2 changes were related to a stimulus-induced change in magnetic susceptibility due the reduced concentration of the paramagnetic species deoxyhemoglobin in venous blood.[18,19] The result was compatible with PET experiments that show large increase in regional cerebral flow and little increase in oxygen utilization.[15,16]

Therefore, there has been an increasing interest from researchers since the BOLD signal was discovered. Consequently, there have been an increasing number of studies about sensorial and, mainly, cognitive paradigms for the understanding of human behavior making it more accessible and quantifiable.

## fMRI and Neuropsychology

Although, researchers are increasingly betting in mapping cognitive performance using fMRI, neuropsychological standardized tests are easy to administer and sensitive to disease-related abnormalities and is, still, the only method to evaluate cognitive deficits in most of the diseases.

Searching the terms "fMRI and Neuropsychology" at the pubmed is possible to find a high number of papers related to several diseases, such as epilepsy, autism, schizophrenia, Parkinson disease, multiple sclerosis, dementias or even healthy volunteers. Those papers aimed to perform fMRI for understanding the structure-cognitive function-localization, the functional connectivity involved with some cognitive function, the language, motor or emotion lateralization and how brain behaves after rehabilitation.

Therefore, we will, briefly, pass through the neurological diseases mentioned above showing some findings related to fMRI and neuropsychology.

## Epilepsy

The fMRI language task is one of the most used protocols performed in patients who undergo brain surgery, in particular epilepsy surgery, to predict language lateralization (LL) and mi-

nimize risks of aphasia after surgery. This method has been used instead of Wada test and dichotic auditory tests, because it is non-invasive, less costly and produces powerful results.[21]

It is possible to find different protocols to measure LL such as: passive words vs. rest, passive words vs. passive tones, semantic decision vs. rest, semantic decision vs. tone decision, semantic decision vs. phoneme decision.[22]

Nowadays, paradigms evaluating memory, visual and somatosensory systems have been used in experimental contexts; however they still have limited clinical application, but demonstrate to be promising.[23]

### Autism

Most fMRI researches have been addressing cognitive control protocols in patients with autism, because of the repetitive behaviors, as well as the higher cognitive manifestations observed during neuropsychological tests.

Then, the fMRI studies of cognitive control have shown anomalous activation in frontoestriatal brain regions[24], which is in accordance with a human structural neuroimaging study that associated cognitive control with frontoestriatal brain systems, including the lateral prefrontal cortex, inferior frontal cortex, anterior cingulate cortex, intraparietal sulcus and striatum.[25,26]

In addition, functional connectivity MRI studies proposed a theory that autism is a "cognitive and neurobiological disorder caused by under functioning integrative circuitry".[27,28]

### Schizophrenia

The cognitive deficits in Schizophrenia are the core feature of the illness and are presented throughout the life span.[29] From the cognitive impairments presented by these patients and neuroimaging studies, researchers concluded that the pre-frontal cortex is affected, because it plays an important role in control-directed behavior, thought and organization,[30] and the functional-based tasks showed an abnormal frontal pole activation.[31,32] Schizophrenia is also a widespread disease, since the fMRI cognitive tasks, such as working memory and also rest-fMRI showed abnormal functional interactions between the pre-frontal cortex and widespread regions of parietal cortex, temporal regions and default mode network.[33,34]

### Multiple sclerosis

The cognitive deficits in patients with multiple sclerosis tends to occur in the early stages of the disease, including impairments associated to attention, information processing speed and working memory, affecting up to 70% of all patients.[35]

Some studies have suggested that fMRI is a valid tool to monitor the therapeutic intervention on cognition, assessing the functional correlates of acute and chronic administration of acetylcholinesterase inhibitors in these patients.[36,37]

There are also researches studying the beneficial effects of cognitive rehabilitation on executive functions and attention associated with compensatory strategies in cognitive-related-network.[38,39]

### Parkinson disease (PD)

The working memory impairment present in PD led Trujillo et al. (2015)[40] to carry out the visuospatial n-back task during the fMRI scan to get evidences of these patients, compared to controls, exhibiting increased task-related recruitment of the left dorso-lateral prefrontal cortex (DLPFC) and decreased functional connectivity of the bilateral DLPFC with brain regions within the networks. They also found altered frontoparietal connectivity with inferior parietal cortex.

Another research group performed the stop-signal task during fMRI, since response inhibition and initiation deficits are also common in PD. The results showed that PD, in comparison to controls, were slower only on response initiation and the task activated the response inhibition network, which includes inferior frontal gyrus.[41]

Although PD is a disorder affecting motor system, Fernandino et al. (2013)[42] demonstrated a functional role of the motor impairment in the comprehension of sentences related to figurative action language.

### Dementia

Cognitive functional MRI studies are difficult to be performed by people with Alzheimer´s disease, because cognition becomes importantly impaired.

Although, mild Alzheimer disease and mild cognitive impairment patients could be able to understand the instructions and be engaged in fMRI task. Therefore, most studies are related to functional connectivity and rest-fMRI.

Notwithstanding, we found a study with semantic dementia that is characterized as a gradual semantic memory loss, preserving the episodic memory, but episodic future thinking impaired. This study by Viard et al. (2014)[43], measured the brain activity in four patients and 12 healthy volunteers during an envisioned future task. They found that the functional integrity of bilateral superior medial gyri and anterior hippocampus are the core for episodic future thinking.

## CONCLUSION

Although the neuropsychological assessment is still the main way to evaluate cognition, since patients complain of difficulties and we can achieve and understand the dysfunctions using just pencil/paper tasks, studies have shown an agreement between neuropsychological deficits and structural neuroimaging findings and now, also, fMRI.

Therefore, the high accuracy of fMRI for assessing cognition leads us to be engaged to use and improve this technique. So, we will be increasingly more confident to associate cognitive dysfunctions with the specific brain areas which will be very useful for surgical proposal, treatment and rehabilitation planning and prognosis.

This brief review underscores the importance of the integration between the classical neuropsychology and fMRI demonstrating their significance for clinical care.

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