Doctoral research project:
Brain specialization for words and numbers:
A high-resolution fMRI-MEG precision imaging study

- Background and scientific questions

Over the past millennia, humans created graphic symbolic systems allowing them to preserve and share cognitive constructs in a durable visual form. Thus words, numbers, and music can all be written down using basic signs and their recursive combinations. This invention rests on plasticity, the brain's ability to change under the effect of experience, and on cortical specialization, the principle of ascribing specific functions to dedicated brain regions. Comparing the alphabetic (ABC…) and the numerical (123…) systems provides a unique access to the relative contribution of bottom-up and top-down processes to the recognition of symbols. Indeed, digits and letters are indistinguishable on the basis of their visual or auditory shape, but they differ widely in the cognitive domains to which they refer.

Cognitive functions exploration and evaluation demands to map diverse spatio-temporal neural dynamics. Either high spatial or high temporal resolution is individually provided by noninvasive neuroimaging technologies such as functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG), but not both simultaneously. A pioneering approach combining MEG and fMRI, MEG/fMRI fusion, has demonstrated the capability to achieve both spatial and temporal resolutions[1].

With a focus on the visual and auditory cortices, **our goal is to explore the use of MEG/fMRI fusion to study the specialization for words and numbers, to understand the role of long-distance influences in the nature and origin of such specialization, and to improve the understanding and potentially the rehabilitation of acquired reading disorders.** Lesions of the Visual Word Form Area (VWFA) [2] yield Pure Alexia, a reading deficit which as a rule affects both words and numbers [3]. However, cases with spared reading of numbers are also on record [4]. Similarly, rare left superior temporal lesions may cause pure word deafness sparing [5], or limited to [6], the comprehension of number names. Such dissociated cases indicate that specialization may exist down to modality-specific cortices for usual words as opposed to number words [5]. The functional imagery literature suggests that indeed a bilateral region in the inferior temporal gyrus, distinct from the VWFA, may be in charge of processing Arabic numerals [7]. However, this putative Visual Number Form Area (VNFA) may actually implement more abstract mathematical processes [8] rather than the identification of symbols. There is currently no consensus on the role of task demands and on format (e.g. 20 vs TWENTY) in the properties of the VNFA. There are no parallel imaging studies on number processing in the auditory cortex.

- Specific objectives

We will develop innovative techniques of MEG/fMRI fusion for the study of brain specialization for words and for numbers, in the visual and auditory cortices. Written stimuli will provide bottom-up input to visual areas and crossmodal top-down input to auditory areas, and conversely for spoken stimuli. Top-down influences will also be manipulated by **varying task demands**. More specific objectives are:
(i) to find **areas of specialization** for alphabetic vs numerical symbols in the visual and auditory cortices using univariate and multivariate methods, **(ii)** to probe the "**representation format**" of such areas by identifying their sensitivity to low- and hi-level features of stimuli such as e.g. font or semantics, **(iii)** to determine whether specialization differs between **bottom-up vs crossmodal top-down** input, **(iv)** to determine whether specialization differs with **task requirements**, **(v)** to assess the prediction that, within specialized regions, top-down and bottom-up influences should predominate in **different cortical layers**, **(vi)** to identify the time-course of those effects using **MEG**, for determining whether task-dependent effects reflect early expectation-driven modulations of bottom-up processes, or late modulatory influences by task demands, **(vii)** to acquire functional resting state and diffusion images in order to distinguish specialized areas on the basis of their **long-distance connectivity** [9,10].

- General methods

Precision imaging. The "precision imaging" approach, based on the collection and analysis of cumulative individual data, gives access to individual-specific functional organization, which is otherwise obscured by group averaging. We will apply this principle to MRI and MEG imaging.
Participants. We will study a set of ~15 individuals, a sample size sufficient for precision imaging, in which statistical analysis is performed on individual data set. Participants will obey the usual inclusion and exclusion criteria for participating in language-related fMRI experiments. Their words and numbers reading ability and calculation proficiency will be assessed individually.
Design. This study will be comprised of 12 experimental conditions, obeying the following fully crossed structure: *Domain (alphabetic / numbers)* ***X*** *Task (low-level / verbal / semantic)* ***X*** *Modality (visual / auditory).* In low-level task participants will either decide whether each word is printed in normal or italic font or uttered by a female

or male voice. In verbal task they will either read or repeat each word aloud. In semantic task they will either decide whether each word refers to an animate or inanimate entity, or decide whether each number is quantitatively larger or smaller than 5555.

MEG/fMRI fusion. This technique generates a common space between different imaging modalities. It matches brain locations characterized with fMRI, and time points characterized with MEG, based on their shared profile of sensitivity over conditions, that is over stimuli, and over experimental tasks.

Laminar resolution. Although still challenging, there is now evidence that it is possible to reach laminar resolution with 7 Tesla fMRI, and to link differences in laminar localization to contrasts between top-down and bottom-up experimental conditions. This project is designed in such a way that it success does not depend on laminar imaging. Nevertheless, we will additionally to try implement this innovative approach, which is relevant to our questioning on bottom-up vs top-down factors in symbols processing.

- Alignment with the institute

The development of MEG/fMRI fusion to explore symbols recognition represents an unprecedented technological innovation. This study will lead to enhanced comprehension of language processing, reading and lexical access. Moreover, medical intervention as well as rehabilitation will increase in relevance. IUIS inclination toward interdisciplinarity meets ICM's core purpose. By allowing scientific and clinicians to work together, this laboratory promotes collaboration between engineering and medical sciences.

Laurent Cohen has a massive background in the study of symbols recognition's neural bases. He will support the theoretical and cognitive questioning. Eric Bardinet brings specific technical expertise to this project. His knowledge and skills are essential to develop the MEG/fMRI fusion.

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