The effects of spatial resolution and physiological contrast on fMRI patterns

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Knowledge valorization

In this thesis, I presented fundamental research in the field of the cognitive neuroscience. In particular, I used functional magnetic resonance imaging (fMRI) to study auditory processing in the brain (Chapter 2 and 3) and investigated benefits and drawbacks of non-standard fMRI techniques, such as arterial spin labeling (ASL; Chapter 3 and 4) and ultra-high field fMRI (Chapter 2 and 4).

The methodologies and findings presented are, therefore, immediately relevant for researchers using fMRI and/or investigating auditory processing. Moreover, in this chapter, I sketch their possible impact outside fundamental research and how they could be valorized in view of societal benefits. *Knowledge valorization* — also known as *knowledge utilization*, *knowledge transfer*, *science impact*, or *third mission of the universities* — has gained increasing importance in recent years till becoming a central element in science policy (Guston, 2000). In line with many scientists' concern about such new policies (Stemerding & Nahuis, 2014), in my opinion, the relevance of scientific research goes well beyond its immediate or short-term outcomes. Even though its commercial value is not its main drive, past history has demonstrated the complex and unpredictable path from scientific research to societal impact (e.g., penicillin, microwave,...). Thus, scientists have to be aware how important it is for society to valorize the acquired knowledge in a broader sense than the pure seek of knowledge. In the light of these considerations, the following paragraphs present some valorization possibilities of the work illustrated in this thesis.

7T (f)MRI: from research to clinical tool

(F)MRI is a non-invasive imaging technique and therefore represents a highly valuable instrument both for research and clinical purposes. As a consequence, any research project, which challenges the current standards of (f)MRI, has the potential also to significantly contribute future clinical protocols, thus benefiting patient populations. Ultra-high field MRI (i.e., above 4 T) are currently employed almost exclusively in research contexts, while hospitals commonly utilize 1.5 and 3.0 T scanners. In the past few years, more and more evidence on the benefits of ultra-high field (f)MRI has been collected by the scientific community. For example, 7 T MRI was proven superior with respect to 1.5 and 3.0 T in delineating the target areas for deep brain stimulation in Parkinson's disease patients and in depicting the microvasculature of brain tumors (van der Kolk et al, 2013; and references therein). However, strong arguments in favor of maintaining the current clinical equipment are their lower cost and easier management. Our outcomes of Chapter 2 and 4 contribute to the accumulating evidences that ultra-high field (f)MRI, thanks to the higher signal-to-noise (SNR) ratio and achievable spatial resolution, provide (the scientist here, but potentially also the clinician) richer and therefore more valuable information on cognitive brain processes in healthy subjects and, by generalizing, also in patients. For instance, an MVPA approach similar to the one presented in Chapter 2 (speech content decoding from high-resolution 7T fMRI signal) may be developed to predict which patients with stroke-induced aphasia are likely to recover and which treatment could benefit them the most (inspired by Crinion et al, 2012).

When to use 7T ASL instead of 3T ASL for brain perfusion measurement?

ASL techniques allow measuring brain perfusion in a quantitative and non-invasive manner. Therefore, ASL has a great potential for the diagnostic and following-up of all those pathologies that affect cerebral blood flow (CBF), such as cerebrovascular diseases, dementia and brain tumors. However, medical doctors are quite resistant to introduce ASL measurements as standard diagnostic exam and they still prefer invasive techniques, such as PET, which requires injection of radioactive tracers, or Gd-DTPA contrast agent injection in MRI. Part of this resistance may be attributed to the large variety of ASL methods that have been developed in the past years making it difficult for a practitioner (e.g., clinicians and MRI technicians) to routinely utilize it in applied projects and diagnostics. For this reason, scientists of the ASL community have joined forces to discuss and achieve a consensus on best practices and recommendations for implementation of ASL in standard clinical context, which have been reported in the so-called *ASL white paper* (Alsop et al, 2015). Our study in Chapter 4 moves the discussion about the "best" ASL implementation a step forward comparing 3T ASL implementations not only among each other but also with a 7T ASL variant. This comparison may become extremely relevant once 7T scanners will become a clinically accepted magnetic field strength. Taking into account a wide range of factors influencing ASL performances, we were able to provide concrete recommendations to guide researchers (and clinicians) in setting up study protocols.

ASL, a new non-invasive approach to tackle tinnitus?

In Chapter 3, we used, for the first time, an ASL implementation to study the frequency processing of the auditory cortex in the human brain and we proved its feasibility. Previous studies have demonstrated that CBF signal offers some advantages (such as higher spatial specificity, quantitative measures, and no venous bias) with respect to the standard blood oxygenation level-dependent (BOLD) signal, although with lower SNR. For this reason, one could think to employ ASL to study pathologies, whose origins and/or mechanisms could not be explained by BOLD studies. Given that we validated the functional sensitivity of CBF signal to frequency auditory processing in the human brain, a possible candidate for such exploratory investigation is tinnitus, which is a disease defined by the perception of a sound in the absence of its corresponding external source. Tinnitus is often associated with concentration problems, sleep disturbance, anxiety, depression and extreme fatigue and in its more severe forms may interfere with people's normal life. Tinnitus is affecting about 16–21% of the adult population and 10–15% of the general population seeks medical attention due to its symptoms. Currently, the underlying mechanisms (pathology) of tinnitus are unknown and no cure is available (Maes, 2014; and references therein). It is therefore evident that it is necessary to continue investigating tinnitus, a research context in which ASL fMRI could contribute to new insights and, possibly, to establish a novel clinical treatment.