NeuroImage 62 (2012) 641–647

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Review

How challenges in auditory fMRI led to general advancements for the field

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ARTICLE INFO

Article history:
Accepted 1 January 2012
Available online 8 January 2012

Keywords:
Clustered volume acquisitions
Sparse sampling
Tonotopy
Auditory cortex

ABSTRACT

In the early years of fMRI research, the auditory neuroscience community sought to expand its knowledge of the underlying physiology of hearing, while also seeking to come to grips with the inherent acoustic disadvantages of working in the fMRI environment. Early collaborative efforts between prominent auditory research laboratories and prominent fMRI centers led to development of a number of key technical advances that have subsequently been widely used to elucidate principles of auditory neurophysiology. Perhaps the key imaging advance was the simultaneous and parallel development of strategies to use pulse sequences in which the volume acquisitions were "clustered," providing gaps in which stimuli could be presented without direct masking. Such sequences have become widespread in fMRI studies using auditory stimuli and also in a range of translational research domains. This review presents the parallel stories of the people and the auditory neurophysiology research that led to these sequences.

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Introduction

The following review presents our personal reflections on the massive collaborative efforts undertaken in the early days of fMRI and how they ultimately resulted in one of the key cornerstones for conducting experiments involving sound presentation — the clustered-volume acquisition (CVA) or "sparse sampling" technique. This technique is predominantly used today to conduct fMRI for the purposes of auditory neuroscience, but has a range of other applications in other sensory and cognitive domains. The two authors started to develop this technique independently, unaware that the inherent problems of conducting auditory neuroimaging in an intensely noisy environment had motivated work that was converging on the same solution. We seek to provide an historical perspective on how this process took place in both Boston and Nottingham.

Our early goals

Tom: "During late 1993, the second entering class of the MIT-Harvard Division of Health Sciences and Technology Speech and Hearing Sciences Program (of which I was a member) visited the MGH-NMR Center, and received a tour from Bruce Rosen. This tour included a brief presentation by Randy Benson about his research investigating the use of fMRI as an alternative to Wada testing for language lateralization (Benson et al., 1999). Having briefly been exposed to the concepts of neuroimaging in a senior elective while at Purdue, I was hooked.

In March 1994 I began to work at MGH, learning about fMRI and how I might apply it to questions appropriate to my graduate program. I quickly concluded that I would take on the task of elucidating

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doi:10.1016/j.neuroimage.2012.01.006

the frequency mapping in the auditory cortex of humans, seeking to demonstrate that the tonotopic maps observed within central auditory fields of cats and monkeys (Merzenich and Brugge, 1973; Merzenich et al., 1973; Morel et al., 1993) were analogous (if not homologous) in man. There was a general consensus in the field that such a finding (e.g., Wessinger et al., 2001) would be of appreciable value to translational research, both from a clinical and basic science perspective, as variations in selectivity for stimulus properties (e.g., amplitude modulation rate; Schreiner and Urbas, 1986, 1988) in experimental animals might then be sought and exploited for the understanding, augmentation or electrical replacement of human hearing. Others at the time were also pursuing similar lines of enquiry (Bilecen et al., 1998; Wessinger et al., 1997).

Working with Randy as my mentor, we conducted our first tonotopy-related experiment in July 1994, modeled after the design of previous works in PET (Lauter et al., 1985) and MEG (Pantev et al., 1988; Romani et al., 1982). This experiment built on pilot data Randy had collected in May 1992, shortly after initial presentation by Tom Brady of Ken Kwong's work in BOLD-fMRI (Brady, 1991). Our initial experiments were not particularly successful, primarily because our subjects could barely hear our stimuli (750 and 2000 Hz tones), even when presented at full volume."

Deb: "Under the leadership and vision of Sir Peter Mansfield, the School of Physics and Astronomy, University of Nottingham, had grown from the mid-60s to the mid-90s into one of the most prestigious centres for biomedical imaging in the UK. Sir Peter's early pioneering work not only transformed NMR into a medical imaging technique, but also foresaw what would be required to make the technique clinically useful. Notably, using the extensive in-house expertise in gradient coil design the group had built the first 3 T MR scanner in the UK using an Oxford magnet. By the time a new centre for NMR was built on the campus in 1991 (later renamed The Sir Peter Mansfield Magnetic Resonance Centre, in honour of his Nobel prize), its head, Peter Morris, was welcoming local collaborative opportunities to pursue new NMR applications in the sensory and cognitive neurosciences. Mark Haggard, Director of the MRC Institute of Hearing Research (MRC IHR) in Nottingham saw the huge potential of this emerging methodology and created a new post for a postdoctoral research scientist to lead a fMRI project in the auditory neurosciences. I started working with Mark in December 1996 to explore the spatiotopic organization of auditory cortex with respect to some of the key sound features such as sound level, modulation, pitch etc. I was soon introduced to Richard Bowtell, a reader in experimental physics with expertise in gradient coil design. Working with Richard and one of his bright young PhD students, Stuart Clare, as my MR physics mentors, I started to learn about fMRI and soon realized the many challenges ahead. Stuart's PhD was focused on developing the technique of fMRI to study visual, motor and auditory brain activation. Under Richard and Peter's watchful eyes together we worked closely for my first couple of years in Nottingham building up sufficient preliminary data to demonstrate to ourselves that we could reliably detect sound-related activity across multiple auditory cortical fields."

Imaging-related acoustic noise

Despite being separated by over 3000 miles, both of us were being rudely introduced to the vexing issue of the acoustic noise associated with MR imaging. The intensity of the ambient noise is exacerbated in the case of the echo-planar imaging (EPI) pulse sequences used for fMRI.

Tom: "Each time the gradients are switched "on" to force a sweep across *k*-space for image acquisition (specifically the "readout" portion), current flows through coils that are wound in a spiral manner, in a plane orthogonal to the generated magnetic field. The moving charges comprising this current undergo a Lorentz force that deforms the coil winding ever so slightly. Because these coils are embedded in a rigid tube, the slight motion results in a slight contraction or expansion of the tube, with an associated dull, "knock"-like sound. During EPI, the current polarity is reversed many times per second to effect a trajectory through the entirety of *k*-space, producing many such sounds in rapid succession. Human hearing has a nominal range of 20 Hz–20 kHz at birth. As long as these "knock" sounds occur in a train with a period that places their repetition frequency in this nominal range, the subject (and experimenter) will experience a pitch percept associated with image acquisition. In the majority of cases (particularly in the early days of fMRI), the imaging systems produced these sounds at intensities approaching 120 dB SPL, frightfully near the threshold of pain. Needless to say, conducting auditory fMRI was rather a challenging activity."

Deb: "The spectral characteristics of the EPI noise are mainly a function of the "readout" gradient pulses of the chosen MR pulse sequence and comprise a series of harmonically related peaks together with a background of broadband noise. Most of the energy is at the lower end of the audible range up to about 1 kHz (see Hall et al., 2009). Both groups in Boston and Nottingham made numerous systematic measures of the noise level. The GE/ANMR scanner at the MGH-NMR Center was found to produce a strong harmonic complex with a fundamental frequency at 1 kHz (Ravicz and Melcher, 1998), while the purpose-built 3 T MR scanner in Nottingham had a dominant peak of acoustic energy at 1.9 kHz (Foster et al., 2000)."

How auditory cortical mapping motivated solutions to imaging-related acoustic noise

On both sides of the Atlantic, we kept thinking about the problems caused by the hostile acoustic environment and kept searching for creative ways to solve them. Our successes were based upon developing effective multidisciplinary relationships with a group of outstanding collaborators who had the expertise to make the study of the auditory system using fMRI something other than quixotic.

Tom: "By late 1994, I had now established my co-advisors as Bruce Rosen and Jennifer Melcher (Eaton-Peabody Laboratory, EPL), and been connected to Mike Ravicz (an engineer at EPL, specializing in acoustics), Patrick Ledden (then a graduate student at MGH, who dabbled in coil construction), and, thanks to Randy, a number of outstanding people at MGH (including Ken Kwong, Robert Weisskoff and Roger Tootell) who would prove invaluable both in this research and in our efforts to improve auditory fMRI. Intervention by these outstanding colleagues and mentors led to three key advancements that facilitated the investigation of tonotopy, and subsequently enhanced our research into perception of speech and other auditory stimuli.

The first was simply avoiding direct masking of stimuli, by shifting our stimulus frequencies away from the 1 kHz frequency of the readout gradient switching. Coupled with this change, Mike had measured the transfer characteristic of the pneumatic stimulus delivery system and reported significant roll-off above 3 kHz. Therefore, we initially limited ourselves to "high" frequencies in the vicinity of 2.5 kHz. While not optimal, we were at least able to present individual frequencies several octaves apart, lending hope that we might resolve different foci of activation for each stimulus.

The second key advancement was a means to present stimuli effectively while also attenuating scanner noise. In our initial experiments, Randy and I simply placed pneumatic delivery headphones over the subject's ears, resulting in 15–20 dB attenuation of the scanner noise, but also resulting in loss of much of the acoustic energy of the stimulus into the cavity between the headphones and the ear canal. Therefore, Jennifer and Mike modified a set of highly-rated ear defenders to connect to the pneumatic delivery system by extending tubing from the pneumatic delivery system through the muffs toward the ear canals, and inserted probe tube ear plugs at the end of