

From Neurons to Behavior

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The present thesis investigated information processing in the human auditory cortex (AC) and the use of computational modeling to bridge information obtained across methods (physiological to behavioral), scales (from single neuron to behavior), and species (human and non-human primates). Furthermore, the presented work generated new datasets and empirical results that can inform, extend, and improve the AC computational models. In the first part of the thesis, we constructed a computational model of the AC that incorporates the parallel information processing pathways along the rostral-caudal axis of the AC. This model links neuronal response properties at the microscale to functional observations at the meso- and macroscale. The model was validated against existing data and then employed to construct hypotheses on the neural correlates of experimental (i.e., behavioral and neuroimaging) observations in human sound perception. In the second part of the thesis, behavioral and neuroimaging techniques were used to detail the visual influences on auditory processing in the AC. Overall, our results suggested distinct roles of the parallel information processing pathways for sound processing and provided evidence for the role of the AC beyond uniquely unisensory processing. Across these studies, both the simulated and observed responses showed interesting variations along the auditory cortical hierarchy, and suggest a prominent role for belt regions in auditory processing of complex sounds and audiovisual processing. In this chapter, we integrate results reported in the individual chapters and discuss follow-up research along with potential future applications.

1 Bridging the Scales: From Neurons to Imaging and Behavior

The computational modeling approach taken in Chapters 2 and 3 primarily intended to link the different scales of empirical observations to each other. Specifically, we focused on the differences in sound processing that exist along the rostral-caudal axis of the AC. This research was fueled by evidence that the areas located caudally and rostrally to the primary auditory cortex exhibit distinct neuronal response properties (Recanzone et al., 2000; Tian et al., 2001; Bendor and Wang, 2008; Camalier et al., 2012; Kuśmierk et al., 2014) which have been proposed to underlie their functional specialization, thus forming the starting points of “what” (rostral) and “where” (caudal) pathways (Kaas et al., 1999; Romanski et al., 1999b; Belin et al., 2000; Kaas and Hackett, 2000; Rauschecker and Tian, 2000; Tian et al., 2001; Arnott et al., 2004). How the differences in neuronal dynamics lead to specific roles in auditory perception, has remained an open question in auditory neuroscience (Jasmin et al., 2019).

The computational model presented in Chapter 2 was built on physiological and electrophysiological observations primarily recorded from non-human primates (Kaas and Hackett, 2000). The model was employed to investigate the contribution of the

different cortical streams in the representation and processing of basic acoustic features (i.e., temporal modulation, pitch) in the context of artificial and natural (speech) stimuli. The model, simulating neuronal populations (operating at mesoscale), replicated human performance in simple psychophysical tasks. Thereby it provided insight on how human auditory perception may be shaped by underlying neuronal responses and which cortical sites might underlie said behavior. The simulations showed more complex computations when moving higher in the auditory cortical hierarchy. This is consistent with the role of belt areas in increasingly complex auditory tasks. That is, while the detection of amplitude modulations in simple artificial stimuli was primarily coded by the simulated core areas of the AC, testing with more complex stimuli showed that the simulated auditory belt (but not core) provided a distributed coding mechanism for temporal and spectral pitch (in the caudal and rostral regions of the simulated belt, respectively). Further analysis with speech stimuli strengthened the idea that the neuronal response properties may be optimized along the rostral-caudal belt to process different acoustical features in parallel, with different simulated regions preferentially coding different oscillatory components of the signal. Interestingly, the slowest oscillations, representing the speech envelope, were coded in parallel across simulated regions and may serve to “timestamp” the traces of different speech aspects belonging to the same speech utterance across streams. This might serve as a binding mechanism that ensures the unified processing of different components of speech (Giraud and Poeppel, 2012; Yi et al., 2019), which may be coded in a distributed fashion. Such a temporal code can also underlie the binding of auditory sources in stream segregation (Elhilali et al., 2009).

Despite being simplistic, the proposed computational model of the auditory cortex offered a general framework for information processing along the rostral-caudal axis in the AC. The model was then used to gain new insights into existing experimental data in Chapter 3. Recent neuroimaging studies have reported a spectro-temporal trade-off along the rostral-caudal belt, i.e., a preference for fine spectral structures of sounds in the rostral regions, in comparison with partiality to fine temporal features of sounds in the caudal regions (Schöwiesner and Zatorre, 2009; Santoro et al., 2014). While the hemodynamic blood oxygenation level-dependent (BOLD) signals measured with functional MRI (fMRI) are correlated to the underlying neuronal activity (Logothetis et al. 2001; Logothetis et al. 1999; Rees et al., 2000), it does not directly measure the neuronal activity. Thus, a forward modeling approach was put forth in Chapter 3 to determine whether the spectro-temporal preferences for sound features along the rostral-caudal streams, inferred from the modeling of fMRI data (Santoro et al., 2014, 2017), could be a direct consequence of the fundamental neuronal mechanisms and response properties. The applied approach combined the computational model of the AC presented in Chapter 2 with a biophysical model of the hemodynamic BOLD response (Havlicek et al., 2015). Our simulations showed that the hemodynamics of

a caudal belt region in the AC were best explained by the neuronal models with faster temporal dynamics and broader spectral tuning, while that of a rostral belt region were best explained through fine spectral tuning combined with slower temporal dynamics. These simulations provided a direct link between observations of neuronal dynamics from electrophysiological recordings (microscale) upon which the model was built, to the BOLD responses (mesoscale). Whereas the observation of BOLD responses provided information about distinct preferences for sound features along the rostral-caudal belt regions, the proposed modeling approach provided insights into the neuronal dynamics that may cause the observed experimental effects.

The modeling endeavors of Chapters 2 and 3 have shown how computational modeling can meaningfully integrate experimental observations, generate new insights into existing datasets, and produce hypotheses for future research. The primary focus of the model was to establish evidence for the role of neuronal dynamics in meso- and macroscale level observations. The model, however, represents a simplification of a complex system and one has to remain cautious of its limitations. Models cannot replace data and the link to empirical observations must be maintained. Also, the models can only suggest or disprove a certain mechanism as a root cause for an observation and will always be reliant on the experimental findings for definitive proof. The simplicity of the current model, which allowed us to manipulate parameters in a well-controlled manner, ignored other key contributors to information processing in the AC. We explored the processing in tonotopic channels, but the influences of non-tonotopic connectivity and multisensory information were essentially disregarded in the current model implementation. Furthermore, the model was strictly feed-forward and modeled no cortico-cortical connectivity beyond the AC. Thus, for the model to grow towards a more “realistic” view of the information processing in the AC, we required deeper exploration of other information arriving in the AC (modulatory or driving influences, feed-forward and/or feedback sources) and how that information interacts with sound processing. Thus, the latter half of the thesis specifically focused on collecting datasets that may shed light on multisensory influences on auditory processing.

2 Visual Influences in the Auditory Cortex

Our environment is highly multisensory, and sounds are almost always accompanied by information from other senses. Recent studies show direct anatomical connections between the early auditory and visual cortices that are concentrated in visual sites representing the far peripheral field of view (Falchier et al., 2002, 2010). The behavioral and cortical correlates of this spatially specific connectivity have, to-date, remained unexplored in humans and were the focus of the research presented in Chapters 4 and 5.

To establish evidence of cross-sensory influences between peripherally-presented audiovisual stimuli, we employed a psychophysical approach in Chapter 4. The bidirectional audiovisual interactions were explored in the far periphery using simple stimuli (gratings and noise bursts; modulated and static) in a modulation detection task. We found evidence of multisensory influences of visual stimuli on auditory reaction times during the modulation detection task, but no reciprocal effects of audition on vision. By manipulating the congruency and the phase of the modulated stimuli (auditory and visual) at the onset of the stimuli, we found that the observed effects were highly sensitive to the temporal structure of the stimuli. That is, depending on temporal (in)congruence and synchrony between modulated audiovisual streams, the visual influences not only sped up (facilitation effects) the response times for auditory stimuli but also slowed them down (degradation effects). These results showed successful multisensory integration but painted a complex picture of underlying neuronal mechanisms, which could rely on direct communication between the early auditory and visual cortices but also influences from higher-order cortical sites.

The study presented in Chapter 5 was driven by the two key results reported in Chapter 4 i.e., the visual influence on audition with no reciprocal effects and, the sensitivity of these effects to the temporal relationship (phase, congruency) between the far-peripheral stimuli. To locate the cortical sites driving these cross-modal observations, we investigated the visual influences on the auditory cortex in a cortical depth-dependent manner using high-resolution functional MRI at 7 Tesla in Chapter 5. Due to the setup constraints of the MRI scanner, the stimuli could not be presented as peripherally as in Chapter 4. Thus, we first tested the spatial dependence of previous observations by repeating the modulation detection task measurements at a less peripheral location. We found evidence of a visual benefit for the auditory modulation detection thresholds even without a cross-sensory phase shift, while this shift was essential for observing a multisensory benefit at the more peripheral location. These results suggested that the exact nature of the audiovisual interactions varies with respect to the location of the stimuli, something that sets up precedence for future research beyond this thesis.

Driven by the task-dependence observed in the behavioral study, these multisensory interactions were explored in two different attention conditions with the hypothesis that by directing attention to the auditory stream, the multisensory effect would be enhanced in the auditory regions. The depth-dependent analysis of high-resolution fMRI data exploits the fact that neuronal populations at different cortical depths have distinct anatomical connectivity and properties. While the sensory input arrives at the middle layers, feedback signals shape predominantly the responses of deep and superficial layers (Felleman and Van Essen, 1991; Winer and Schreiner, 2011). These distinct columnar properties can be reflected in the independent responses across cortical depths and are

measurable because of the sub-millimeter resolution of the fMRI data (De Martino et al., 2015; Moerel et al., 2018; Gau et al., 2020). Our preliminary analyses showed a significant multisensory enhancement of responses across a cortical network including the primary and non-primary auditory cortex, the left primary and non-primary visual cortex (contralateral to stimulus location), bilateral insular cortex, and the ventrolateral prefrontal cortex. In the AC, the multisensory enhancement increased along the auditory cortical hierarchy and was strongest in the superior temporal gyrus, which likely reflects the auditory parabelt. While multisensory influences (enhancement and suppression) were present throughout layers of the AC, the multisensory enhancement was modulated by attention in the deep layers of the auditory belt. This effect was only observed when directing attention towards the auditory stimulus and was absent when the attention was diverted away from both stimulus streams. This modulatory effect of attention in deep layers, rather than middle layers, suggests that this context-dependent multisensory influence originates as a feedback signal. Where this feedback originates, remains to be determined. Some possible candidates could be tertiary auditory regions, visual cortex, or frontal regions. However, the tertiary auditory regions are not a likely source of the observed effects as short-range feedback more strongly targets the superficial than deep layers (Clavagnier et al., 2004). Future analyses will include multivariate pattern analysis to examine the multisensory effects in a multivariate fashion, and cortical depth-dependent connectivity analysis which may help discriminate between the frontal regions and visual cortex as sources of the observed context-dependent multisensory enhancement in deep layers of the auditory belt.

How do the observed cross-sensory influences on AC processing relate to the parallel processing streams of the AC explored in the first half of this thesis? The increased multisensory enhancement in the deep layers of belt areas when attention is directed to the auditory stimulus is of particular interest. The multisensory effect observed in Chapter 4 is driven by congruency in spatial location and temporal features of the auditory and visual stimuli. Our modeling approaches presented in Chapter 3 suggested that the caudal belt regions are optimized for capturing temporal sound dynamics. We, therefore, hypothesize that the attentional influence on multisensory processing targeted caudal instead of rostral belt regions. Moreover, beyond processing the temporal dynamics of auditory stimuli, we hypothesize that caudal belt regions may process the temporal dynamics of their multisensory counterparts as well. In line with these hypotheses, the direct projections from peripheral primary and secondary visual cortex have been shown to target caudal auditory regions (Falchier et al., 2010). These hypotheses may be in part addressed through further analysis of the dataset reported in Chapter 5. Electrophysiological experiments will also be required to fully test these hypotheses, as these measurements are needed in order to shed light on the temporal mechanisms of multisensory integration of peripheral audiovisual stimuli.