APAN 2017 TALK ABSTRACTS

KEYNOTE LECTURE

Prof. Jennifer Groh, Duke University

Hearing in a world of light: The why, where, and how of connecting visual and auditory information in the brain

No sensory system is an island. The auditory and visual systems work together to provide information about the nature of the events occurring in the environment. I will talk about why they do this, where in the brain it happens, and how the brain performs the necessary computations to achieve it. I will emphasize the following general insights:

1. Interactions between sensory systems occur at the earliest possible point in the auditory pathway, namely, the eardrum.

2. The brain may employ a strategy called time-division multiplexing, in which neural activity fluctuates across time, to allow representations to represent more than one simultaneous stimulus.

These findings speak to several general problems confronting modern neuroscience. For example, textbook descriptions of the brain describe it as a hierarchically organized feed-forward system, with the interesting stuff happening at some pinnacle of the pathway. Early interactions between sensory systems undercut this view. Secondly, the time-division multiplexing hypothesis suggests a connection between variability in neural signals and otherwise unexplained limits in perceptual, attentional, and working memory capacity.

YOUNG INVESTIGATOR SPOTLIGHT

Dr. Josh McDermott, Department of Brain and Cognitive Science, MIT

Computational Neuroimaging of Human Auditory Cortex

Just by listening, humans can determine who is talking to them, whether a window in their house is open or shut, or what their child dropped on the floor in the next room. This ability to derive information from sound is enabled by a cascade of neuronal processing stages that transform the sound waveform entering the ear into cortical representations that are presumed to make behaviorally important sound properties explicit. Although much is known about the peripheral processing of sound, the auditory cortex is less understood, particularly in humans, with little consensus even about its coarse-scale organization. This talk will describe our recent efforts using computational neuroimaging methods to better understand the cortical representation of sound. I will present new evidence for functional segregation in non-primary auditory cortex, for representational transformations occurring between primary and nonprimary cortex that may support the recognition of speech, music, and other real world sounds, and for computational frameworks that can account for these transformations. The work has been enabled by several technical innovations in stimulus design and fMRI analysis, including the generation of model-matched stimuli, sound quilting, voxel decomposition analysis, and the use of deep neural networks as models of auditory computation. These developments will be described along with the empirical results they have enabled.

1 Motor cortex suppresses auditory cortical responses to self-generated sounds

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One often wants to ignore the sounds of their own movements, such as the sound of their own footsteps, to focus on environmental cues. Filtering out self-generated sounds requires that the brain forms an internal model that selectively suppresses neural responses to sounds that are reliable consequences of certain movements, such as footsteps, finger tapping, or vocalizing. Consistent with such a predictive mechanism, indirect and population-level recordings in primates and songbirds suggest that auditory cortical responses to self-generated sounds are selectively attenuated. Moreover, correlative studies suggest that this predictive suppression may be mediated by motor cortical inputs to the auditory cortex. Although motor cortical inputs are capable of generically suppressing auditory cortical activity during a wide variety of movements, whether these inputs selectively suppress auditory cortical responses to self-generated sounds, and the synaptic mechanisms through which this predictive suppression may arise, remain unknown.

To address these questions, we developed an acoustic virtual reality (aVR) platform to study how the mouse cortex learns to predict the sounds associated with a movement. Following several days of aVR experience during which locomotion triggered a series of tones with fixed pitch, auditory cortical excitatory neurons became largely unresponsive to predictable self-generated sounds, yet they retained their responsiveness to locomotion-triggered sounds at other frequencies. Mice exhibited a perceptual blind-spot for tones matching the self-generated pitch when they were locomotion, but not for other sound frequencies and not when they were resting. In contrast to excitatory neurons, auditory cortical inhibitory neurons responsive to the training tone displayed enhanced movement-related activity after several days of aVR experience. Notably, long-range excitatory projections from the motor cortex are an important source of movement-related recruitment of auditory cortical inhibitory neurons. One possibility is that aVR experience selectively strengthens motor cortical drive onto auditory cortical neurons that are responsive to the locomotion-associated pitch. Consistent with this idea, we found that aVR experience strengthened connections between the motor cortex and auditory cortical interneurons that were responsive to the self-generated pitch, resulting in the selective motor-related recruitment of a tuned-subset of inhibitory neurons. These findings are consistent with a framework in which motor-related signals, and their interaction with local auditory cortical circuitry, can predictively suppress neuronal responses to self-generated sounds."

2 Plasticity in cortical fast-spiking GABA networks supports recovered sensory processing following peripheral nerve injury

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The adult sensory cortex exhibits a remarkable plasticity following damage to sensory organs. Afferent denervation results in a reorganization of cortical maps, a rebalance of network activity and changes in sensory capabilities. These compensatory adaptations have been associated with reduced GABA signaling and cortical hyperexcitability. However, it is unknown how functional modifications in sensory processing and dynamic changes in intracortical inhibition relate to one another during this process. Here, we directly measure changes in parvalbumin-expressing (PV) GABA networks in the adult auditory cortex (ACtx) and relate changes in local inhibition to recovered auditory processing in putative pyramidal (PPy) neurons after a near-complete loss of cochlear nerve afferents. We describe two approaches: 1) An optogenetic strategy to monitor daily changes in the net strength of PV-mediated feedforward inhibition and 2) a chronic cellular imaging approach to directly visualize changes PV and PPy neurons.

For the first approach, we made chronic recordings from individual PPy units in the ACtx of awake, head-fixed mice while optogenetically activating PV neurons for a 7-8 week period surrounding profound auditory nerve damage. This approach allowed us to compare distinct forms of plasticity, such as spontaneous rate, sensory gain, PV-mediated inhibition and receptive field plasticity, in single PPy units with day-by-day resolution. We found that whereas the status of brainstem-evoked potentials and traditional biomarkers of central auditory hyperactivity did not predict the recovery of sensory responses to surviving nerve fibers, homeostatic adjustments in PV- mediated inhibition during the first days following injury could predict the eventual recovery of cortical sound processing in PPy neurons weeks later. Our findings show a rapid loss and recovery in PV- mediated inhibition that may compensate for a sudden drop in afferent drive and support the progressive recovery of sensory processing.

Findings from our optogenetic experiments reveal striking inhibitory dynamics in the first week after auditory nerve injury but are agnostic as to whether these changes reflect postsynaptic changes in PPy neurons or changes in the PV networks themselves. Our ongoing experiments use chronic 2-photon calcium imaging to simultaneously visualize sound-evoked GCaMP signals in genetically identified PV neurons alongside neighboring PPy neurons. Collectively, our work identifies the central importance or rapidly releasing the PV plasticity ‘brake’ to enable recovered sensory processing in the adult cortex following injury."

3 A critical role of inhibition in temporal processing maturation in the primary auditory cortex

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Faithful representation of sound envelopes in primary auditory cortex (A1) is vital for temporal processing and perception of natural sounds. However, the emergence of cortical temporal processing mechanisms during development remains poorly understood. Although cortical inhibition has been proposed to play an important role in this process, direct in vivo evidence has been lacking. Using loose-patch recordings in rat A1 immediately after hearing onset, we found that stimulus-following ability in fast-spiking (FS) neurons was significantly better than in regular-spiking (RS) neurons. In vivo whole-cell recordings of RS neurons revealed that inhibition in the developing A1 demonstrated much weaker adaptation to repetitive stimuli than in adult A1. Furthermore, inhibitory synaptic inputs were of longer duration than observed in vitro and in adults. Early in development, overlap of the prolonged inhibition evoked by two closely following stimuli disrupted the classical temporal sequence between excitation and inhibition, resulting in slower following capacity. During maturation, inhibitory duration gradually shortened accompanied by an improving temporal following ability of RS neurons. Both inhibitory duration and stimulus-following ability demonstrated exposure-based plasticity. These results demonstrate the role of inhibition in setting the pace for experience-dependent maturation of temporal processing in the auditory cortex.

4 Representations of tones in core fields of monkey auditory cortex depend on their associated, upcoming behavioral outputs during the performance of auditory tasks

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Representations of sensory stimuli in sensory cortex depend on a variety of factors that are crucial for converting the stimuli into appropriate behavioral outputs during goal-directed tasks. However, an understanding of the effects of behavioral outputs themselves on sensory representations has been elusive. Here, by conducting a study in two nonhuman primates in which they performed two auditory tasks, we show that tone representations in core fields of auditory cortex depend on the upcoming behavioral outputs associated with the tones. The tasks were performed on the same set of stimuli and had a symmetrically rewarded go/no-go structure. The tasks and the stimuli were designed in such a way that the same tones could be associated with different behavioral outputs, i.e., making a bar release (go response) or withholding a bar release (no-go response), in different tasks. The same tones could also be irrelevant to making the appropriate behavioral outputs in the tasks. Neuronal activity evoked by the same tone differed when it was associated with an upcoming go or no-go response. The differences were observed in the spike activity of ~25% of the 420 multiunts and in the local field potentials at ~85% of the 570 sites recorded in core fields of auditory cortex. In both the spike activity and local field potentials, such differences emerged mainly because of increased activity evoked by the tone when it was associated with a no-go response and barely changed activity when it was associated with a go response, relative to that when it was irrelevant to making an appropriate behavioral output. Our results suggest that tone representations in core fields of auditory cortex can change to reflect whether an upcoming go or no-go response should be made to the tones, i.e., auditory cortex can attach behavioral meaning to the tones."

5 Electrocorticographic investigation of auditory predictive coding in the human brain across levels of consciousness

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Predictive coding models of sensory processing emphasize the integration of feedforward and feedback information streams across the sensory cortical hierarchy. Studies employing local/global deviant (LGD) stimulus paradigms (e.g. Bekinschtein et al., 2009, PNAS 106:1672-7) offer promise for elucidating the neural basis of sensory awareness. Non-invasive studies show that responses to local (within-trial) deviance are robust to changes in the level of consciousness, whereas responses to global (across-trial) deviance are not. Non-invasive recordings offer limited opportunity to investigate the contributions of specific cortical regions to these processes. This study used electrocorticography (ECoG) to refine the localization of LGD responses and test their sensitivity to loss of consciousness (LOC) under general anesthesia.

Subjects were neurosurgical patients undergoing removal of intracranial electrodes placed to identify epileptic foci. Stimuli were four repetitions of a vowel, followed by the same or different 5th vowel (local deviant; LD). Global deviance (GD) was manipulated by varying the percentage of “same” and “different” patterns. The stimuli were presented during an awake baseline period and during induction of general anesthesia with stepwise increases in propofol dose. The subjects were instructed to respond to GD stimuli with a button press. ECoG recordings were made with depth electrodes implanted in the superior temporal plane and subdural grid electrodes implanted over the hemispheric convexity. Analysis of cortical responses focused on event-related potentials (ERPs) and high gamma (70-150 Hz) power.

Changes in ERP amplitude associated with LD were broadly distributed across temporal, frontal and parietal regions. High gamma responses to LD were more spatially restricted and localized primarily to auditory cortex in the superior temporal plane and on the lateral surface of the superior temporal gyrus. During induction of general anesthesia, LD effect became progressively more restricted to auditory cortex and, within core auditory cortex, was resistant to LOC. GD effect was most prominently seen in non-core auditory cortex, surrounding auditory-related and prefrontal areas, and had longer latencies than the LD effect. Induction of general anesthesia led to an early abolishment of GD effect.

These data demonstrate differential effects of general anesthesia on preattentive (LD) and higher-level predictive coding (GD) mechanisms of novelty detection in the human auditory cortex. LOC is associated with early suppression of higher-level predictive coding processes, followed by attenuation of preattentive components of auditory novelty detection.

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6 Single-neuron correlates of spatial attention and choice in auditory and prefrontal cortex

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Auditory spatial attention describes our effortless ability to listen to sound from one location while suppressing distracting sounds from other locations. Two key areas implicated in this ability are auditory cortex and prefrontal cortex, but a detailed understanding of how sound is spatially filtered has been hampered by the lack of a robust animal model, particularly one that shares key similarities with humans. To address this, we have developed a novel spatial auditory selective attention task for macaques, based closely on human directed listening paradigms. In this task, a macaque monkey is cued to a particular side and must report the presence of a difficult-to-detect auditory target (embedded in noise) only if it appears on the cued side. If it appears on the uncued side, he must ignore it.

We collected single neuron data from prefrontal cortex (caudal principal sulcus; n=948) and caudal auditory cortex (primarily A1; n=847) in two monkeys during this task. In both areas, direction of cued side significantly affected responses in about 20% of the neurons. A comparison of patterns between PFC and AC indicated that AC was earlier than PFC in signaling the sensory stimulus (ipsi/contra), but PFC was earlier than AC in signaling the decision made (release/ignore). We applied a classification approach on firing rates of the responsive populations to analyze patterns of firing rates related to error (e.g. misses) vs correct trials, This indicated that the first location to exhibit patterns of activity that classified significantly lower than correct was in AC during the masking noise period. Thus, at least some errors are due to an inability to suppress noise at the level of sensory cortex. These results add insight into the cortical dynamics of auditory decision making during effortful listening.

7 Frequency-decoding of omitted sounds using MEG illustrates tonotopic specificity of predictions in the human auditory system

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Sensory stimuli in our environment are usually presented in a distinct context, making certain features more or less predictable. Predictions can work independently from voluntary attentional focusing and usually go along with reduced neural responses to predictable events. An interesting phenomenon in the auditory system is the demonstration that omissions of predicted sounds lead to pronounced responses in auditory brain regions, functionally putatively reflecting prediction error processes. Furthermore it has been previously shown that the extent to which an omission is predictable, has an impact of the magnitude of the so-called omission response. In the current MEG study (N = 25), we seek to understand whether predictions in the human auditory system act in a tonotopic specific manner. For this purpose we used pure tones of four different carrier frequencies to create (Markov chain) sequences of different entropies, resulting in one ordered, one random and two mid-entropy level sequences. Sounds were presented at a 3 Hz rate while participants watched a silent movie. Importantly, in 10% of the presentations a sound stimulus was omitted. By applying MVPA to the sound and silent (omission) periods we assessed whether sound frequency could be decoded and what impact the entropy level played for decoding performance. Decoding sound frequency using the real sounds (i.e. training on sound, testing on sounds) shows this can be done reliably virtually on a single-subject, with an overall accuracy of ~40% (25% chance level). Entropy had an influence in a sense that best decoding performance was obtained during random sequences, while worst decoding was seen for the regular sequence. More importantly however, applying decoding to the omission periods (training on sounds) increases of decoding accuracy in particular when the tone sequence was ordered, with an early (< 70ms) and a late (~100-120ms) portion, likely reflecting processes related to predictions and prediction errors. Overall, this study provides strong evidence that top-down predictions in the auditory system, also in absence of focused attention, impacts auditory activity in a sound frequency specific (i.e. tonotopic) manner.

8 Neural encoding of attended speech in primary and non-primary human auditory cortices

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Humans posses the ability to segregate one speaker from another, even when there is no spatial separation between them. Invasive human neurophysiology studies have revealed a spectro-temporal representation of an attended speaker in non-primary auditory cortex (superior temporal gyrus; STG) that rapidly changes depending on the attentional focus of the listener. However, how such a representation emerges in STG is unknown. In addition, the representation of speech in primary auditory areas (Heschl's gyri; HG) remains unexplored due to their inaccessibility from the surface. Here, we used invasive depth electrodes and surface recordings to investigate the neural encoding of attended speech along the auditory cortical pathway.

Subjects listened to a male and female speaker, both in isolation (single-speaker; S-S), and mixed together (multi-speaker; M-S), with no spatial separation between them. To characterize the tuning properties of each electrode site, we obtained their spectro-temporal receptive field (STRF). Electrodes in HG tended to respond at short latencies (~50 to 150ms) and were narrowly tuned, with some electrodes responsive to speaker-specific features (e.g., the fundamental frequency of the male speaker). These electrode sites retained this speaker-selectivity, even when that speaker was not being attended to. Electrodes in STG responded at longer latencies (~150 to 300ms), were more broadly tuned, showed relatively little speaker-selectivity, and responded preferentially for the attended speaker. Comparing the STRFs from the S-S condition with the M-S condition, the tuning properties of HG electrodes remained similar, whereas electrodes in STG changed their tuning to enhance the attended speaker and suppress the unattended speaker. These results provide a descriptive account of how the acoustic features of attended and unattended speech are progressively processed along the auditory cortical pathway.