APAN Advances and Perspectives in Auditory Neuroscience

Sponsored by TDT and NIDCD

Wyndham Chicago Grand Riverfront, Chicago, IL

Friday, October 18th, 2019

Abstracts

T1 Functional segregation of the marmoset auditory cortex by data-driven decomposition of responses to naturalistic sounds with wide-field optical imaging

Yueqi Guo (1), Xindong Song (1), Chenggang Chen (1), Xiaoqin Wang (1)

(1) Department of Biomedical Engineering, Johns Hopkins University"

The common marmoset (Callithrix jacchus) is a highly vocal New World monkey species and has garnered considerable interest in recent years as a promising non-human primate model in neuroscience. To study the functional organization of the auditory cortex using this animal model, we developed techniques to perform multi-scale and multi-modal chronic optical imaging in awake marmosets. The imaging interface is a removable artificial dura (AD) based window with a diameter of 1/4 inches that covers the region between the lateral sulcus (LS) and superior temporal sulcus (STS). While previous studies have extensively evaluated neural activities in the core region of auditory cortex driven by pure tone stimuli, how the auditory cortex is spatially organized to process naturalistic sounds, especially in the secondary auditory areas, is still poorly understood. In this study, we used a hypothesis-free data-driven method to probe the functional organizations of the marmoset auditory cortex. This method was first developed by Norman-Haignere et al. (2015) for human fMRI studies. We played the same set of 165 naturalistic sounds to marmosets and measured activities in the auditory cortex with wide-field optical imaging. In contrast to the pure tone responsive area (mostly limited to the core region), this set of sound stimuli activated more lateral areas in marmoset auditory cortex (presumably the belt and parabelt regions), suggesting that the secondary auditory areas are sensitive to higher-order features in naturalistic sounds. With the matrix decomposition method used in Norman-Haignere et al. (2015) study, we found independent components located in both primary and secondary auditory areas that were sensitive to different sound features and sound categories. This approach provides a potential way to reveal new functional areas in the auditory cortex of non-human primate. In addition, we analyzed trial-to-trial variance of the responses to the natural sound stimuli. Some lateral areas showed neural activities that were more variable than areas closer to the lateral sulcus (putative core region) under the same stimulus context, suggesting that the activities in these areas may be influenced more by internal processing or the state of the animal, rather than solely dependent on stimulus driven responses.

T2 Allocentric sound localization in ferrets

Stephen Town (1), Jennifer Bizley (1)
(1) University College London

The ability to localize sounds is critical for both human and non-human hearing. Humans can describe sound position within coordinate frames defined by the observer (head, eyes, etc.) or environment. Whether other animals perceive sound location in multiple reference frames is unclear and particularly if animals can report sound location in world-centered reference frames. Neurons within the ferret auditory system represent both head-centered and world-centered (allocentric) sound location, implying that world-centered auditory perception could exist in this species.

Here, we tested whether ferrets could perceive world-centered sound location within a two-choice allocentric sound localization task. Within the task, subjects reported the positions of one of two speakers located at opposite sides of a test arena. Trials were initiated and test sounds presented while the animal was at a central response platform located equidistant between sound sources so that the response ports and sound sources were not co-located. Across trials, the central platform was rotated to prevent use of sound location cues relative to the head or eyes.

Ferrets identified the location of sound sources at each platform rotation and thus reported sound location in the world independently of sound angle relative to the head. Generalization of sound location across head direction occurred immediately after platform rotations, indicating that ferrets did not rapidly re-learn head-centered cues to solve the task. Instead, our results show that ferrets developed a rule-based strategy based on the absolute position of sounds in the world, independent of head orientation. Finally, presentation of probe sounds at novel, untrained locations revealed that ferrets judged sound location on a continuum across space rather than as discrete spatial categories.

Together, our work suggests that like humans, other animals can also perceive sound location in allocentric coordinates. This opens the door for future recording of neurons in the auditory system to understand how neural circuits support coordinate frame transformation of sound space across the brain.

T3 The posterior tail of striatum plays an important role in tonal associative learning

Miaomiao Liu (1), Hanqing Wang (1), Tianyu Li (1),Yiwei Wang (1), Dongqin Cai (2), Kexin Yuan (1)
(1) Tsinghua University (2) Harvard University

The striatum is traditionally divided into three subdivisions based on connection and function, including dorsomedial striatum, dorsolateral striatum, and ventral striatum. These subdivisions are critically involved in various brain functions, including associative learning. Very recently, the posterior tail of the striatum (TS) started to be considered as the fourth subdivision because of its independent dopamine source, and the understanding of its function is still very limited. Although a few studies have shown the essential role of TS neurons in learned discrimination task, whether and how these neurons might play a specific role during associative learning remains unknown. To address this question, we adopted a Go-Nogo behavioral task, in which mice learn to associate one tone with reward (sucrose water) and the other tone with punishment (air puff). We firstly expressed GCaMP6 in the TS of Vgat-ires-Cre mice, then we made fiberphotometry recordings from TS neurons expressing GCaMP6 during the training. We found that the medial and lateral part of the TS showed differential responses to tonal cues. The medial part demonstrated significantly stronger adaptation to tones in the first day of training than the lateral part did.. To find out whether difference in connection might account for the difference in neural responses, we used retrograde mono-transynaptic rabies virus to identify the inputs of medial and lateral TS. We found that the lateral part received more inputs from the auditory cortices, while the medial part received substantially more inputs from somatosensory cortices. Our immunohistological results showed that medial TS is rich of D1R neurons and almost absent of D2R neurons, while lateral TS has more D2R neurons than D1R neurons, suggesting that D2R neurons, which are located laterally, might be more important for associative learning using tonal cues. To test this hypothesis, we optogenetically activated either D1R or D2R neurons during training. We found that both the activation of D1R and D2R neurons significantly accelerated learning process by improving the performance of correct rejection. However, the improved performance was preserved after days of light stimulation only in mice received D2R activation. The performance of mice received D1R activation dropped to control level in the first day of light-off. These data suggest that TS neurons are indeed involved in tonal associative learning, and that D2R neurons might play a more important role.

T4 General auditory and speech-specific contributions to cortical envelope tracking revealed using auditory chimeras.

Kevin Prinsloo (1), Edmund Lalor (2)
University of Rochester

Over the past few years research on natural speech processing has benefited from recognizing that low frequency cortical activity tracks the amplitude envelope of natural speech. This has been useful for investigating the mechanisms underlying speech processing, how such processing is affected by attention, and how audio and visual speech interact. However, it remains unclear to what extent these cortical measures reflect higher-level speech-specific processing versus lower-level processing of the spectrotemporal/acoustic stimulus dynamics. There has been somewhat equivocal evidence that speech intelligibility affects these envelope tracking measures, suggesting that they may indeed index speech-specific processing. These findings have led to the suggestion that different neural populations, having different functional roles in receptive speech processing, may simultaneously contribute to envelope entrainment measures. In the present study, we aim to disentangle contributions to cortical envelope tracking that derive from general auditory processing of acoustic input from those that are functionally related to processing speech. To do so, we presented subjects with “auditory chimeras” – a previously introduced technique that involves modulating the temporal fine structure (TFS) of one speech stimulus, with the amplitude envelope (ENV) of another speech stimulus. This can be done after splitting each stimulus into different numbers of complementary frequency bands, which allows a measure of control over which speech stimulus is actually recognized by the listener. We presented such chimaeric stimuli to subjects as we recorded their EEG. As we decreased the number of frequency bands in the chimaerae, subjects lost the ability to recognize the ENV speech stimulus and began to recognize some of the TFS stimulus. In line with this, the EEG tracking of the ENV stimulus dropped, but remained quite strong, and the EEG began to track the envelope of the TFS stimulus. These results highlight that, while cortical tracking of the speech envelope is largely driving by the acoustic energy of the sound, it contains contributions from speech-specific processing.

T5 Neuromodulation Enhances Plasticity in a Rodent Model of Cochlear Implant Use

Erin Glennon (1), Jasmin Multani (1), Mario Svirsky (1), Robert C. Froemke (1)
(1) New York University School of Medicine

Rates of auditory perceptual learning and asymptotic speech perception performance with cochlear implants are highly variable across patients. Adaptation to cochlear implants is believed to require neuroplasticity within the central auditory system. However, mechanisms by which behavioral training enables plasticity and improves outcomes are poorly understood. Here we investigate the hypothesis that neural mechanisms that promote plasticity in the rodent auditory system are key to optimizing cochlear implant usage, and might be especially helpful in cases of poor performance. We focus on noradrenergic modulation of rat auditory cortex by the locus coeruleus, which can enable robust and long-lasting neural and behavioral changes.

We developed a new surgical approach for cochlear implantation in adult rats. Our approach allows insertion of an 8-channel electrode array covering up to 360 degrees in the cochlea and allows rats to freely behave while using the implant to perform auditory tasks. Rats are trained on a go/no-go task, and self-initiate trials to respond to a target tone. Previously, we showed in normal hearing animals that this task requires auditory cortex, and that this task is sensitive to cortical modulation and plasticity.

Here we examined the effect of pairing locus coeruleus stimulation with an auditory stimulus on auditory learning when the animal has to relearn a tone identification task using a cochlear implant. Initial training was done using acoustic stimuli in normal hearing animals. Animals were then bilaterally deafened and unilaterally cochlear-implanted. Next, animals were retrained on the auditory task with the new target delivered by intracochlear electrical stimulation. Prior to each daily behavioral training session for the new target, one group of rats underwent a 5-10 min pairing session. Pairing accelerated learning with cochlear implants compared to animals that did not receive it. We then conducted multi-unit recordings in the auditory cortex to assess activation of the cortex by the cochlear implant. Animals that had been trained with the cochlear implant had more effective activation of the cortex, and those that underwent pairing had a sharper representation of the target cochlear implant channel. We used fiber photometry to monitor activity of noradrenergic locus coeruleus neurons. During auditory learning, normal hearing animals display dynamic locus coeruleus activity, specifically during the acquisition of the new meaning of reward relevant tones. These studies indicate that neuromodulation can play a powerful role in shaping outcomes with cochlear implant use and training.

T6 Encoding of natural sounds in the aging human auditory cortex

Julia Erb (1) Lea-Maria Schmitt (1) Jonas Obleser (1)
(1) Institute of Psychology, University of Lübeck

Current models of auditory cortical processing describe the neural response to natural sounds as a function of complex acoustic features. Here, we ask whether and how cortical responses to those acoustic features change over the life span. We acquired 3T-fMRI data while young and older adults listened to a story presented against a competing stream of resynthesized natural sounds. We modelled the fMRI responses in auditory cortex as a function of the spectro-temporal modulations contained in the sound mixture, and derived single- and multi-voxel modulation transfer functions (MTFs; fMRI encoding and decoding). We found that topographical best feature maps were preserved in the aged auditory cortex: Tonotopic maps showed the typical mirror-symmetric frequency gradients along Heschl's gyrus in both age groups. Decoding yielded highest accuracies at low frequencies of 230–580 Hz, coarse scales of 0.25 cyc/oct, and slow rates of 4–8 Hz, irrespective of age. However, we observed age differences in tuning to temporal rate, with signatures of broadened rate tuning in older participants. These results indicate that the specificity of temporal representation declines in the aged auditory cortex.

POSTERS

1 Auditory representation in cortex during perceptual learning

Kathleen A Martin (1,2,3), Robert C Froemke (1,2,3,4,5,6)
(1) New York University Neuroscience Institute
(2) New York University Center for Neural Science
(3) New York University School of Medicine Skirball Institute
(4) New York University School of Medicine Department of Otolaryngology
(5) New York University School of Medicine Department of Neuroscience and Physiology
(6) Howard Hughes Medical Institute Faculty Scholar

During perceptual learning, animals improve their ability to discriminate between sensory stimuli. This behavioral improvement occurs at variable rates across animals. Previous work in the auditory system showed that perceptual learning reliably enhances cortical representations of task-relevant stimuli in trained animals. These neural changes have predominantly been observed outside of the behavioral context and regardless of learning rate. However, our lab recently found that engagement in behavior alters auditory cortical responses. Neural and behavior discrimination over perceptual learning are correlated. How do sensory representations change over auditory perceptual learning?

To address these questions, we assessed neural dynamics over learning during behavior within each mouse. We developed an appetitive, head-fixed auditory perceptual learning two-alternative forced-choice task for mice. Animals learned to lick a left lick port for tones of a chosen frequency (usually 11 or 13 kHz) and right for tones of other frequencies to obtain water rewards. This allowed us to probe both auditory acuity and categorical responses over perceptual learning. Animals improved their discrimination between center and surround frequencies over the course of weeks (9-21 days), but continued to make errors on frequencies close to the center frequency. Bilateral muscimol infusions in auditory cortex of trained mice substantially reduced behavioral performance. We performed two-photon calcium imaging of excitatory neurons, inhibitory neurons, and cholinergic axons in auditory cortex throughout learning, to assess neural activity both during this behavior and passive listening. In the behavioral context, many excitatory neurons exhibited a categorical response to the auditory stimuli, not simply encoding the frequency of the stimulus, but rather the behavioral meaning. This categorical response was present early in behavioral learning, but was broader, mirroring the behavioral performance.

2 Top-down and bottom-up expectations in the prefrontal and auditory cortices

Lalitta Suriya-Arunroj(1,2), Yale E. Cohen(1,2,3), Joshua I. Gold(2)
(1) Department of Otorhinolaryngology-Head and Neck Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
(2) Department of Neuroscience, University of Pennsylvania, Philadelphia, PA, USA
(3) Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA

Auditory perceptual decision-making is affected by expectations that can be established via both bottom-up and top-down processes. For example, bottom-up sensory processing can reflect regularity violations in the temporal sequencing of auditory stimuli, whereas top-down processing can encode learned task statistics. However, it is not well understood how these different processes interact in the brain to shape the interpretation of auditory signals that form perceptual decisions. The goal of this study was to investigate the interaction between bottom-up and top-down processing in the auditory cortex and prefrontal cortex. These brain regions were selected because they are part of the ventral auditory pathway, which has a key role in auditory perception and decision-making.

To test these interactions, two rhesus monkeys listened to a sequence of high-frequency or low-frequency tone bursts that were embedded in background of broadband noise. The monkeys reported whether the last tone in each sequence (the “test tone”) was low or high frequency by pulling or pushing a joystick, respectively. We titrated task difficulty by varying the sound level of the test tone relative to the noisy background. We manipulated bottom-up expectations by presenting three identical low or high frequency tone bursts (“pre-tones”) to establish a sequence regularity that either was or was not violated by the immediately succeeding test tone. We manipulated top-down processing by presenting, before sequence onset, a visual cue that indicated the prior probability (“pre-cue”) that the test tone would be high or low frequency within a given block of trials (corresponding to ratios of low- versus high-frequency test tones of 3:1, 1:1, or 1:3).

The monkeys’ behavioral choices and response times were affected by both the pre-tones and the pre-cue. Ongoing analyses of neural data are assessing the interactions between top-down and bottom-up processes in the auditory cortex and prefrontal cortex that are responsible for these effects of different sources of expectations on auditory decision-making.

2 Human speech cortex encodes amplitude envelope as transient, phase-locked responses to discrete temporal landmarks

Katsuaki Kojima (1), Yulia Oganian (1), Chang Cai (1), Anne Findlay (1), Edward Chang (1), Srikantan Nagarajan (1)
(1) University of California San Francisco

The slow (1-10Hz) temporal amplitude envelope of speech reflects acoustically and perceptually relevant information about speech temporal structure and content, including syllabic structure. It is well-established that the phase of neural activity in the delta-theta bands (1 - 10 Hz) is aligned to the phase of the speech amplitude envelope during listening. This has been taken as evidence for continuous entrainment of endogenous low-frequency oscillations to the speech envelope, possibly driven by phase-reset at some landmark event in the envelope, such as local peaks in the envelope (peakEnv) or times of rapid increases in amplitude (peakRate).

We recently showed using direct electrocorticography (ECoG) that local neural populations in speech cortical areas selectively encode peakRate events in continuous speech. This finding suggests that peakRate is the primary envelope cue represented in speech cortex. However, it leaves open whether phase-locking of low-frequency oscillatory activity observed with M/EEG reflects these transient responses. Alternatively, it might reflect the phase-reset of endogenous oscillatory activity by either peakRate or peakEnv events. We predicted that if it reflects transient responses, phase-locking would 1) rapidly diminish between consecutive acoustic edge events and 2) cover a frequency range reflective of the temporal structure of the speech stimulus envelope. In contrast, if phase-alignment reflects phase-reset of ongoing oscillatory activity, it should continue for several cycles between consecutive acoustic edges and its frequency range should be independent of stimulus envelope dynamics.

To contrast these predictions, we recorded neural activity using MEG while participants (n = 12) listened to regularly-paced and 1/3-slowed continuous speech. We analyzed the phase of neural activity in the delta-theta band (1 - 10Hz) over bilateral temporal regions, aligned to acoustic edges and peaks in the speech envelope. Phase-locking was increased when neural activity was aligned to peakRate events, more than it was aligned to peakEnv events, replicating our intracranial results. Crucially, phase-locking in lower frequency bands increased for slowed speech compared to regular speech. Finally, phase-locking peaked after peakRate events and diminished within a single cycle. This pattern of phase-locking is suggestive of an underlying transient response, rather than continuous oscillatory entrainment. These results were robustly evident at the single subject level.

These data confirm and extend our previous intracranial findings to low-frequency activity and provide a link between results from intracranial electrophysiology and non-invasive MEG recordings. Taken together, our results demonstrate that the speech envelope induces a series of evoked responses at times of rapid increases in the speech amplitude envelope, rather than continuous alignment of intrinsic oscillatory activity.

4 Representation of behavioral integration time downstream of auditory cortex

Justin Yao (1), Justin Gimoto (2), Dan Sanes (3)
(1) New York University
(2) New York University
(3) New York University

The central representations of environmental signals are transformed at each locus of an ascending sensory pathway. One characteristic of this hierarchical processing is that the time required to fully encode a sensory cue (i.e., integration time) increases at ascending levels of the nervous system. Here, we sought to determine how auditory information is transformed downstream from core auditory cortex (ACx), at a location thought to support sensory decisions, the parietal cortex (PC). Gerbils were trained and tested on an appetitive alternative forced-choice (AFC) auditory temporal integration task. Specifically, gerbils were required to discriminate between amplitude modulated (AM) noise at 4 versus 10 Hz across a range AM durations (100-1000 ms). Behavioral integration times were measured by examining how AM discrimination scales with stimulus duration. Task performance was poor at very short AM durations (100-200 ms), improved with longer durations, and reached an optimum at ~600 ms. To determine the downstream projections from gerbil ACx to PC, viral tracing experiments were performed. The data revealed a disynaptic pathway from ACx to dorsal auditory cortex to PC. Thus, we hypothesized that the integration times for AM cues are transformed downstream from ACx, in PC, thereby creating the representation that supports integration time on the AM task. To test this idea, muscimol was bilaterally injected in PC to attenuate activity during task performance. While animals continued to perform the task following muscimol infusion, integration times were increased. To determine whether a PC encoding mechanism could account for these behavioral results, we conducted wireless recordings of single-unit activity from neurons in ACx and PC while gerbils simultaneously performed the auditory temporal integration task. Neural integration times are calculated from discharge patterns obtained during psychometric performance. We predict that ACx integration times for AM signals will be significantly shorter than those displayed behaviorally, whereas the neural representation in PC will yield integration times that match psychometric performance. Collectively, these experiments will reveal whether the neural representation downstream of ACx, in PC, is necessary and supports the observed behavioral temporal integration times.

5 Musical training enhances cortical phase-locking while listening to continuous naturalistic speech

Sebastian Puschmann (1), Mor Regev (1), Sylvain Baillet (1), Robert J. Zatorre (1)
(1) Montreal Neurological Institute, McGill University

There is increasing evidence that musical training can benefit the perception of speech in noise (Coffey et al., 2017). Previous electrophysiological work suggests that this "musician advantage" is related to superior low-level sensory encoding of auditory input in musicians, leading to more robust and more distinct cortical representations of speech (Du & Zatorre, 2017; Parbery-Clark et al., 2012). However, whether musical training also benefits speech processing beyond sensory encoding is still largely unknown.

We used Magnetoencephalography (MEG) source imaging and an inter-subject phase-locking analysis to test whether musical training benefits the functional coupling between auditory cortices and higher-order brain regions during the perception of naturalistic speech. MEG data were obtained from 20 individuals (age: 21±3 years) with a varying degree of musical training (duration: 0-18 years) while listening to a continuous audio story (duration: 15 minutes) without background noise.

While listening to continuous speech, subjects showed robust inter-subject phase-locking between auditory cortices and a broad ensemble of other brain regions of the adjacent temporal, frontal and parietal lobes, in both hemispheres ($p<.05$, FDR). This effect was consistent for the delta (i.e., 1-4 Hz), theta (4-8 Hz) and alpha (8-12 Hz) bands. Musical training was associated with increased alpha-band phase-locking between bilateral auditory cortex and the dorsal and ventral speech processing streams (Spearman correlation; $p<.05$, FDR). Importantly, musical training enhanced auditory cortex phase-locking to both ipsi- and contralateral brain regions, suggesting a more bilateral processing of speech information in musically trained individuals.

Our results suggest that the previously reported "musician advantage" in speech-in-noise processing may not only arise from a more robust low-level encoding of speech information, but also from a stronger functional coupling between the auditory cortex and higher-order brain areas involved in speech processing.

References

Coffey EB, Mogilever NB, Zatorre RJ. 2017. Speech-in-noise perception in musicians: A review. Hear Res 352, 49-69.
Du Y, Zatorre RJ. 2017. Musical training sharpens and bonds ears and tongue to hear speech better. Proc Natl Acad Sci USA. 114:13579–13584.
Parbery-Clark A, Tierney A, Strait DL, Kraus N. 2012. Musicians have fine-tuned neural distinction of speech syllables. Neurosci 219, 111-119.

6 Rats and VRats: using virtual rats to study the behavior and neural activity of freely moving rats in a complex environment

Alex Kazakov (1), Maciej M. Jankowski (1), Ana Polterovich (1), Johannes Niediek (1) Israel Nelken (1,2)"   "

(1) Edmond & Lily Safra Center for Brain Sciences, The Hebrew Univ. of Jerusalem, Israel

(2) The Silberman Institute of Life Sciences; The Hebrew Univ. of Jerusalem, Israel

Reinforcement learning together with deep learning (RL-DL) is a powerful paradigm for solving real-world control problems. We developed two parallel setups to investigate biological and computational reinforcement learning – The first one is a large interactive environment (RIFF, rat interactive fantasy facility; diameter, 1.6 m) where rats train to maximize rewards (food/water) over time. The RIFF operates according to a Markov Decision Process, based on the rat location and activity. The rats interact with the arena via 12 ports, comprised of a food or water dispenser, an air-puff valve and a nose poke detector ("interaction areas", IAs). The rat is tracked in real-time by a ceiling-fixed camera (30 Hz). We taught adult rats (Sabra, female, N=5) to behave as instructed by different sounds that are presented in the RIFF, in order to maximize rewards (food/flavored water) and to avoid air-puffs. The rats performed hundreds of short trials (10-30 seconds, each ending with a reward or a punishment) in a single session (1 hour long, over many weeks). Neural responses were recorded from insular or auditory cortices by 16 tungsten electrodes (flexDrive) with a Neurologger system (Deutron). The other setup is an in-silico replica of the RIFF, a computer model that performs similar tasks under similar environmental laws and constraints. The full observability of the virtual setup allows us to develop hypotheses that we test on the biological one. The RIFF was replicated in-silico as a 2D arena with similarly located IAs, driven by the same MDP. The virtual rat (VRat) is modeled as a point inside this arena, with constraints on acceleration and turns to resemble the biological rat. The VRat brain is comprised of an artificial neural network (Deep Q-Network, 300 neurons in total) that emits an action based on the observed state. The VRat was trained through reinforcement learning, and converged to near-optimal policies that were surprisingly similar to the policies of the biological rat as compared by reward return, trajectory features and action distribution. We currently investigate what causes the rats and VRats to converge to similar policies, and to what extent the internal representations (as judged by neural responses in the rats and by the full state of the neural network in the VRat) are related to each other.

7 Synaptic zinc contributes to contrast adaptation in auditory cortex

Patrick A Cody (1), Thanos Tzounopoulos (2)
(1) Department of Bioengineering, University of Pittsburgh
(2) Pittsburgh Hearing Research Center and Department of Otolaryngology, University of Pittsburgh

Phenomena of sensory adaptation have been extensively described but understanding of the underlying synaptic mechanisms trails behind. A common function of sensory adaptation is to maintain a signal percept amid changing contexts. This is, at least in part, accomplished via contrast gain control, a process in which instantaneous firing-rate gain compensates for changes in background stimulus contrast, or variance. In auditory cortex this process modulates the sensory evoked response to the sound level contrast within which a signal is presented: the signal response amplitude increases with decreasing variance in sound level of background noise. We assay this phenomenon with 2-photon calcium imaging in layer (L) 2/3 of mouse primary auditory cortex (A1) to investigate the biological mechanisms involved in this specific form of sensory adaptation termed contrast gain control. Consistent with previous studies, A1 L2/3 principal neurons adapt their sound evoked responses to the sound level contrast and duration of the background noise preceding the signal. We find that modulation to contrast was limited to A1 L2/3 principal neurons displaying monotonically increasing sound level tuning curves, termed monotonic neurons. Contrast modulation also depended on the location of the signal sound frequency within neuronal receptive fields as well as within the context frequency bandwidth. Because synaptic zinc has emerged as a cell-specific modulator of response gain and tuning in A1 L2/3 neurons, we tested whether it contributes to contrast adaptation. We found that upon zinc chelation, responses were no longer greater in low contrast relative to high contrast; high contrast responses increased while low contrast responses remained consistent. Synaptic zinc thus contributes to elevated low contrast responses via inhibition of responses in high contrast. These findings reveal that synaptic zinc has a physiologically relevant impact on sound perception related to sensory adaptation and begin to approach a synaptic mechanism driving contrast adaptation in auditory cortex.

8 **Human Neural Envelope Coding is Predictive of Speech Intelligibility in Noise**

Vibha Viswanathan (1), Hari M. Bharadwaj (1,2), Barbara G. Shinn-Cunningham (3), Michael G. Heinz (1,2)
(1) Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN
(2) Department of Speech, Language, & Hearing Sciences, Purdue University, West Lafayette, IN
(3) Carnegie Mellon Neuroscience Institute, Carnegie Mellon University, Pittsburgh, PA

Models of speech intelligibility that accurately reflect human listening performance across a broad range of background-noise conditions are important both clinically (e.g., for deriving hearing-aid prescriptions, and optimizing cochlear-implant signal processing), and for evaluating speech-processing algorithms in technological applications (e.g., in mobile phones). A leading hypothesis in the field is that internal representations of envelope information ultimately determine intelligibility. Consistent with this hypothesis, envelope-coding based models of speech intelligibility in noise have been widely successful. However, this hypothesis has not been tested neurophysiologically. Here, we address this gap by combining human electroencephalography (EEG) with simultaneous perceptual intelligibility measurements. First, we derive a neural envelope-coding metric (ENVneural) from EEG responses to speech in multiple levels of stationary noise that span the full range of intelligibility from 0 - 100%, and identify a mapping between the neural metric and corresponding speech intelligibility. Then, using the same mapping, we use only EEG measurements to test whether ENVneural is predictive of speech intelligibility in novel background noises and in the presence of linear and non-linear distortions. Our results suggest that neural envelope coding is predictive of speech intelligibility for different realistic listening conditions. However, we also find that neural envelope coding in the central auditory system may depend on factors other than peripherally-available envelope cues. These results inform modeling approaches based on neural coding of envelopes, and may lead to the future development of physiological assays for characterizing individual differences in speech-in-noise perceptual abilities.

9 Role of top-down inputs in auditory cortex during vocalization in marmoset monkeys

Steven J Eliades (1), Joji Tsunada (1)
(1) University of Pennsylvania

Human speech is a sensory-motor process involving auditory self-monitoring to control vocal production and ensure accurate communication. Monitoring auditory feedback during vocal production allows one to quickly adjust speech to compensate for perceived changes in vocal output, a control behavior shared with many animal species. The auditory cortex has been implicated in this self-monitoring process based upon previous studies showing both a suppression of the auditory cortex during vocal production as well as sensitivity to changes in vocal feedback. However, the mechanisms of this vocalization-induced suppression in auditory cortex remain poorly studied. We recorded neural activity from the auditory cortex of marmoset monkeys while they produced self-initiated vocalizations, analyzing both spiking activity and local field potentials. We found that previously-demonstrated pre-vocal suppression of neural firing is associated with an increase in low-frequency theta-band activity. We further show that, for many neurons, the magnitude of pre-vocal spiking suppression correlates with the acoustics of the subsequent vocalization. These findings suggest that this pre-vocal input to the auditory cortex, presumably a top-down signal, contains specific information predicting the expected sound of a vocalization, consistent with current models of feedback vocal control. Additionally, we found that gamma-band oscillation activity increases during vocalization, in contrast to suppression at single- and multi-unit levels. This dissociation between spiking activity and local field potentials further implicates local processing within the auditory cortex as a possible mechanism of vocalization-induced suppression.
This work was supported by NIH/NIDCD Grant K08-DC014299."

10 Behavior of freely moving rats in a complex environment modeled by reinforcement learning with informational constraints

Johannes Niediek (1), Maciej M. Jankowski (1), Ana Polterovich (1), Alex Kazakov (1), Israel Nelken (1, 2) "
(1) Edmond & Lily Safra Center for Brain Sciences, The Hebrew University of Jerusalem, Israel
(2) The Silberman Institute of Life Sciences, The Hebrew University of Jerusalem, Israel

Behaviors of rats in natural environments vary in complexity and in their effectivity in reward collection. We used a large interactive environment ("RIFF", rat interactive fantasy facility; diameter, 1.6 m) in which freely moving adult female Sabra rats (N = 5) obtained food or water rewards from 12 ports. Rats had to time their motion and their nose-pokes according to different sounds in order to obtain rewards and to avoid air-puffs. At all times, rats could choose between several action sequences that differed in both complexity and reward sizes. The RIFF operates as a Markov Decision Process (MDP), where each of the rat actions shifts the environment from one well-defined state into another well-defined state. The theory of MDPs allows to find optimal policies which maximize the reward rate. In order to model behavioral complexity, we added to the MDP's value term a complexity term, where a learned policy's complexity is measured as the Kullback-Leibler divergence between the learned policy and a simple default policy. The model produced a family of policies that differ in their complexity, and realize the optimal reward rate at any given complexity. In the RIFF, all rats learned policies that ensured high reward rates, and different rats discovered different policies. Moreover, these policies shifted within 90-minute recording sessions. A model with information constraints qualitatively captured these different policies. Using likelihoods of recorded trajectories with respect to optimal policies of varying complexity, we estimated actual trade-offs between value and complexity. The shifting policies within sessions were reflected by a concurrent monotonic decrease of their complexities for the best-fitting optimal policies. Our results show that informational constraints are a promising approach for behavioral modeling, even in a scenario where the number of possible actions is high. It provides a large selection of optimal policies that capture much of the observed variability during a session and across animals in a uniform way. Since it is derived from first principles, it can readily be used in a wide range of applications.

11 Multisensory Responses in Primary Auditory Cortex of the Cat

Catherine Boucher (1), Xiaohan Bao (1), Yaser Merrikhi (1), M. Alex Meredith (2), Stephen G. Lomber (1)
(1) McGill University
(2) Virginia Commonwealth University

Core auditory cortex of the cat is comprised of primary auditory cortex (A1) and the anterior auditory field (AAF). Neurons in both fields respond strongly to acoustic stimuli and are tonotopically organized. In hearing animals, a small number of cells in AAF respond to tactile stimulation. Following early-onset hearing loss, a much larger proportion of neurons in AAF become responsive to tactile and/or visual stimulation, indicating that crossmodal sensory reorganization is robust in this core auditory area. Unfortunately, results from similar studies conducted in A1 of the cat are not as clear. In hearing cats, most studies do not show multisensory responses in A1 (Stewart & Starr, 1970; Rebillard et al., 1977; Kral et al., 2003). Furthermore, only one study has documented crossmodal plasticity in A1 following perinatal hearing loss (Rebillard et al., 1977), while others have not (Stewart & Starr, 1970; Kral et al., 2003). A methodological consideration of these studies involves the type of anesthetic used. In this study, hearing animals were lightly anesthetized with ketamine. We recorded audiovisual responses from A1 (i.e., unisensory auditory, unisensory visual, subthreshold multisensory or bimodal) and we examined the visual characteristics to which A1 maximally responds. Multisensory stimuli were developed by pairing a pure tone stimulus with a flash stimulus at various stimulus onset asynchronies, and the visual stimuli presented include gratings, flashes, dots, and checkerboards. A linear multielectrode array recorded multi-unit activity and local field potentials across cortical layers. Contrary to previous work using other anesthetics, we identified unisensory auditory, unisensory visual, bimodal, and subthreshold multisensory multi-unit activity in A1. We also found neurons where auditory-visual interactions either suppressed or enhanced neuronal activity. Additionally, visual stimulation can modulate the neural response to auditory inputs depending on the stimulus onset asynchrony. Taken together, it is possible to identify visually responsive neurons in A1 of the cat. These results will serve as baseline data for a future study, examining the degree to which this cortical area undergoes crossmodal plasticity following early-onset hearing loss.

12 Quantitative Delineation of Sub-regions of Marmoset Auditory Cortex using Ultra-high Field MRI

Yang Zhang(1), Xiaoqin Wang(1)

(1) Department of Biomedical Engineering, The Johns Hopkins University, Baltimore, Maryland 21205, USA

Marmoset is a highly vocal and social New-World monkey of growing interest in neuroscience. It has unique advantages as a non-human primate model for studying neural mechanisms underlying vocal communication and brain functions for social interactions. Understanding anatomical and functional organizations of marmoset auditory cortex is crucial to unveil the mechanisms of auditory perception. Auditory cortex of non-human primates has been divided into core, belt, and parabelt sub-regions. However, the borders between sub-regions defined by histology are usually drawn without quantification. In this study, we developed a method to quantitively define sub-regions of marmoset auditory cortex using ex-vivo multi-modal magnetic resonance imaging (MRI) based on T2-weighted and multi-shell diffusion images. We combined multiple MRI contrasts (orientation dispersion index, fractional anisotropy, principle direction and T2 signals) to provide a multi-dimensional feature space for delineation and validation of sub-regions in auditory cortex. Comparing to previous ex-vivo MRI studies that typically need several days of scan, we were able to obtain high resolution data (0.15mm isotropic) with a small surface coil covering the superior temporal gyrus in about 3 hours on a 11.7T Bruker MRI scanner. A unique feature of our method is that it does not require averaging data from multiple brains and thus can be applied to an individual brain. The method we have developed in this study has the potential to be applied to in-vivo studies in marmosets and can be applied to other cortical areas or other animal species.

13 Neural modulation to direction and speaker in spatial multi-talker speech perception

Prachi Patel (1) (2), Jose L. Herrero (3) (4), Ashesh D. Mehta (3) (4), Nima Mesgarani (1) (2)
(1) Mortimer B. Zuckerman Mind Brain Behavior Institute, Columbia University
(2) Department of Electrical Engineering, Columbia University
(3) Hofstra Northwell School of Medicine
(4) The Feinstein Institute for Medical Research

Humans can attend to speech of a talker in an acoustically complex, spatially separated multi-talker environment. How the human auditory cortex encodes speech of simultaneous spatially separated talkers and how attention to the location of a talker modulates the neural response is unknown. Here, we record intracranially from the auditory cortex of subjects engaged in a listening task with two simultaneous spatially separated talkers, and each spatial single talker stand alone. We demonstrate that the location of speech played in quiet has little effect on the fidelity of its encoding in the human auditory cortex, however, irrespective of attention, in the presence of spatial interfering talker the neuronal tuning narrows to the speech of contralateral talker. Moreover, we show what aspects of the neural response are modulated by attention to the direction of the talker and by attention to the pitch of the talker. Our results demonstrate how the neuronal tuning changes in presence of spatially competing talkers and how the spatial auditory attention modulates the neuronal response.

14 Neural evidence of location constancy for auditory spectral processing in marmoset auditory cortex

Yi Zhou(1), Jonas Braasch(2)
(1) Arizona State University (2) Rensselaer Polytechnic Institute

The computational demands for disassociating sound location (‘where') and spectral feature (‘what') information from each other pose a unique problem for audition. In a naturalistic environment, the signal entering the ear canal is the sum of the direct sound wave from the source and attenuated, delayed reflections from nearby surfaces. One well-known example of this is pinnae filtering. The interference between direct and reflected sound waves attenuates and amplifies signal energy in a frequency-dependent manner, depending on the spatial locations of the source. It remains unknown to what extent the location-related spectral filtering affects spectral processing in the auditory system. In this study, we investigated the effects of varying sound source location on the frequency selectivity of individual neurons in the marmoset primary auditory cortex (A1). The experiment first tested the spatial tuning functions of a neuron to best-frequency tones and broadband noises (100-500 msec duration) over 360 degrees in the horizontal plane. Then the frequency tuning function was evaluated for sound sources presented from four opposite quadrants: contralateral-frontal, contralateral-rear, ipsilateral-frontal, and ipsilateral-rear. We found that cortical neurons across cortical layers show diverse spatial selectivity in the peak direction and width of their spatial tuning. Varying sound location modulates the response gain of A1 neurons. However, their frequency selectivity, such as harmonicity sensitivity, remains largely unaffected across the four spatial quadrants. These results suggest that A1 frequency tuning remains insensitive to spectral perturbations of pinna filtering. The gain-modulation between spatial vs. spectral tuning appears necessary to the dissociation between ‘what' and ‘where' information to achieve location constancy in auditory object perception.

15 Sequence Learning in Mammals: An Animal Model to Explore the Mechanisms of Language Acquisition

Dan LUO(1), Ryszard AUKSZTULEWICZ(1,2), Jan W.H. SCHNUPP(1)
(1) City University of Hong Kong, Hong Kong
(2) Max Planck Institute for Empirical Aesthetics, Frankfurt, Germany

The ability to segment a stimulus sequence in a continuous auditory stream into separate chunks is critical to humans and other animals. In humans, sequence learning ability is likely one of the building blocks of language acquisition, and infants are capable to detect novel stimuli in a continuous speech stream after passive exposure to familiar stimuli [1]. Non-invasive studies in humans suggest that low-frequency cortical entrainment to the rate of presentation of speech segments is modulated by language familiarity [2]. Interestingly, also primates [3] and rodents [4] have been suggested to be able to chunk acoustic streams. Here, we test whether low-frequency entrainment mediates auditory chunking in rodents.

In this study, we trained female Wistar rats (N=7) to perform sequence familiarity discrimination of synthetized acoustic syllable triplets in two-alternative forced choice tasks. First, rats were trained to differentiate 3 single repeatedly presented syllables ('familiar') from their scrambled counterparts, generated anew in each trial ('unfamiliar'). Then, single syllables were replaced with 3 triplets, and rats were trained to discriminate familiar triplets from unfamiliar triplets. Finally, rats were anaesthetized and implanted with electrocorticographic electrode covering their auditory and frontal regions. Rats in a control group (N=7) were passively exposed to familiar stimuli. During electrophysiology experiments, rats were presented with continuous streams of familiar triplets as well as streams containing unfamiliar stimuli. We tested (1) whether cortical activity could entrain to the triplet presentation rate (showing a difference between familiar and unfamiliar triplets), and (2) whether this effect was modulated by active vs. passive training.

Our behavioral data show that rats were able to discriminate familiar syllables and triplets from the reshuffled stimuli. In the electrophysiology data we observed a robust difference in cortical responses to familiar vs. unfamiliar triplets in actively trained rats. For passively exposed rats, the effect of triplet familiarity on cortical activity was diminished. These results suggest that rats can chunk continuous stimulus streams into reproducible segments following active training.

Reference

[1] Saffran JR, Aslin RN, Newport EL (1996). Science 274(5294):1926–1928.
[2] Ding N, Melloni L, Zhang H, Tian X, Poeppel D (2015) Nature Neuroscience 19(1):158–164.
[3] Hauser, M. D., & Fitch, W. T. (2004). Computational constraints on syntactic processing in a non-human. Science, 303, 377–380.
[4] Murphy RA, Mondragon E, Murphy VA (2008) Science 319(5871):1849–1851."

16 **The neural basis of auditory restoration for familiar zebra finch song**

Margot C Bjoring (1), C Daniel Meliza (1,2)
(1) University of Virginia, Department of Psychology
(2) University of Virginia, Neuroscience Graduate Program

Understanding speech in a noisy environment requires an auditory system capable of restoring occluded speech sounds based on word knowledge and contextual cues. This phenomenon, known as phonemic restoration, has been well characterized in humans, but the neural basis of restoration has received less attention. Songbirds make an ideal model for studying auditory restoration at a neuron level because of their acoustically complex vocalizations which are used for tasks like recognition and mate selection in a noisy colony environment. In speech, phonemic restoration is stronger for native than foreign words, and we hypothesize a similar effect for the songs of familiar and unfamiliar birds. To test this, we modified established paradigms for inducing phonemic restoration of speech to zebra finch song and housed subjects in different social groups, which created different sets of familiar and unfamiliar song. We tested the ability of zebra finches to perform auditory restoration using an operant task. We then analyzed the difference in single-unit responses to identify a neural signature for the restoration of familiar vocalizations. We predict that this signature of restoration will emerge within the auditory processing pathway at a site that merges ascending and descending information, and we have identified the caudal mesopallium (CM) and the caudomedial nidopallium (NCM), both secondary cortical-like auditory areas in the avian auditory system, as potential candidates.

17 Birdsong syllable recognition with sparse spike sequence representations

Leonardo Estêvão Schendes Tavares (1), Dezhe Z. Jin (2)
(1) Pennsylvania State University
(2) Pennsylvania State University

Birdsongs consist of sequences of stereotypical syllables. For species such as the Bengalese finch and the canary, song sequences are variable and can follow elaborate probabilistic rules. To study the structure and neural basis of birdsongs, it is critical to label large numbers of syllables from continuous recordings of individual birds. Since manual labeling is tedious and time consuming, a number of standard machine learning techniques have been applied with varying degrees of success to automate syllable recognition. Artificial deep neural networks (DNNs) in particular, the state of the art in automatic speech recognition, can be trained to achieve very low error rates [1,2]. But the high performance comes at the expense of some limiting factors. DNNs require large numbers of pre-labeled training syllables, which directly translates into intensive manual labor. They also often need specialized hardware such as GPUs for training. In practice, most DNN implementations actually rely on sequence information to achieve low error rates. This is undesirable if the goal is to analyze the sequence itself.

Here we present an alternative approach for labeling birdsong syllables from continuous recordings. Most importantly, we have designed our method to minimize the number of training exemplars required. We make no use of sequence information and rely completely on pattern recognition. No special hardware is required.

In our method, we represent relevant sounds by sparse spike sequences of feature-detecting neurons. This approach has been previously shown to perform well in noise-robust speech recognition [3]. Two distinct ensembles of feature detectors are trained by support vector machines (SVMs) to respond to specific acoustic features. Given a continuous recording, one set of non-linear SVMs performs the discovery, segmentation, and initial classification of syllables. Meanwhile, a second set of linear SVMs produces sparse sequences of spikes from the discovered segments, which are then compared to pre-trained templates of spike patterns to check and correct the initial labels. Using only 10 training exemplars per syllable type, we achieve a 5% error rate on Bengalese finch songs. Our system can be efficiently trained and run on basic computers, and requires little technical expertise from the user. As more syllables are classified, our system can be re-trained online to further reduce the error rate.

We have encoded our method into an open-source software in Python for the community to use.

[1] Koumura et. al. (2016). [2] Nicholson and Cohen. Tweetynet. [3] Schafer and Jin. (2014)"

18 MEG correlates of periodicity relevant to pitch perception in human auditory cortex

Seung-Goo Kim (1)*, Tobias Overath (1,2,3,4,5)*, Will Sedley (6), Sukhbinder Kumar (5,6), Sundeep Teki (5), Timothy D. Griffiths (5,6)
* Joint first authors.
(1) Department of Psychology and Neuroscience, Duke University, Durham, North Carolina, 27707, United States
(2) Duke Institute for Brain Sciences, Duke University, Durham, North Carolina, 27707, United States
(3) Center for Cognitive Neuroscience, Duke University, Durham, North Carolina, 27707, United States
(4) UCL Ear Institute, University College London, London, WC1X 8EE, U.K.
(50 Wellcome Trust Centre for Human Neuroimaging, Institute of Neurology, University College London, London, WC1N 3BG, U.K.
(6) Institute of Neuroscience, Newcastle University Medical School, Newcastle upon Tyne, NE2 4HH, U.K.

Pitch is a property of many sounds for which the cortical substrate is still debated. In this study we used MEG to estimate neural ensemble activity in sensor and source space using three types of periodic stimuli at rates below and above the lower limit of pitch. The stimuli were harmonic complex tones (HC), click trains (CT) and iterated rippled noise (IRN). Trials consisted of noise-periodic-noise (NPN) or periodic-noise-periodic (PNP) segments in which the periodic segment was either above (250 Hz) or below (20 Hz) the lower limit of pitch. For ten healthy volunteers (age = 26 ± 7, 5 females), neuromagnetic responses while listening to NPN and PNP trials were recorded using a 274-channel MEG system (CTF systems), and T1-weighted MR images were acquired. Using the MNE Python package, source activity of evoked responses was estimated.
The pitch-associated periodic stimuli (at 250Hz) were all associated with marked evoked responses at ~130 ms at both sensor and source levels after the NP transition (repeated-measures ANOVA, $p < 0.02$). Evoked responses for PN transitions were much weaker (HC, CT) or absent (IRN). The non-pitch-associated stimuli (at 20 Hz) were associated with weak or absent evoked responses at ~130 ms after the NP transition. On the supratemporal plane, evoked responses in Heschl's gyrus showed the greatest peaks, particularly to NP transitions in 250-Hz trials involving HC and CT.
The data demonstrate cortical sensitivity to periodicity associated with pitch that is consistently present across different pitch-associated stimuli in the region of HG.

19 Reorganization of intrinsic neural networks associated with tinnitus

Somayeh Shahsavarani, Rafay A. Khan, Sara Schmidt, Yihsin Tai, Fatima T. Husain
University of Illinois at Urbana–Champaign

Resting-state functional magnetic resonance imaging (fMRI) has been widely used to investigate the organization of intrinsic neural networks and its correlation with neurological disorders. Here, we investigated the association between a hearing disorder, namely tinnitus, and reorganization of intrinsic neural networks. Tinnitus is a condition in which patients perceive sounds in the absence of an external source. The tinnitus patient population is highly heterogeneous in terms of etiology, age, hearing sensitivity, and severity of symptoms. Previous studies from our lab showed that tinnitus was associated with reduced coherency in the default mode network (DMN) and changes in the dorsal attention network (DAN). In this study, resting-state fMRI data were obtained for 10 minutes from a relatively large group of participants including 47 patients with tinnitus (19 females; 79% with hearing loss; mean age = 52.59 years) and 30 controls without tinnitus (15 females; 40% with hearing loss; mean age = 47.73 years). Using Tinnitus Functional Index (TFI) scores, tinnitus patients were divided into those with mild tinnitus (TFI < 25; n=31) and those with bothersome tinnitus (TFI >= 25; n=16). Preprocessing was performed using Statistical Parametric Mapping software (SPM12). Seed-based analysis was conducted to compute resting-state functional connectivity using the Functional Connectivity Toolbox (Conn) while accounting for age, hearing status, and tinnitus severity. Four resting-state networks were investigated: (1) DMN, (2) DAN, (3) the auditory network, and (4) the salience network. The results showed that there were no significant differences between patients and normal hearing controls for all the networks. Compared with hearing loss controls, bothersome tinnitus was correlated with increased coupling between the DMN and supramarginal gyrus (a part of the task-positive network), and mild tinnitus was associated with reduced functional connectivity between DAN and right superior frontal gyrus (a region that plays a role in attention orientation), indicating tinnitus-related changes in both DMN and DAN. Moreover, patients with mild tinnitus showed greater functional connectivity between the salience network and lateral occipital cortex than hearing loss controls. Patients with bothersome tinnitus also showed greater functional connectivity between the salience network and precuneus (a major hub in DMN), relative to those with mild tinnitus. Our findings highlight the importance of non-auditory intrinsic networks including DMN, DAN, and the salience network in differentiating tinnitus from non-tinnitus groups and for indexing severity.

20 **Eye movement is linearly encoded by eardrum motion: the decipherable EMREO**

David LK Murphy (1), Cynthia D. King (1), Stephanie Schlebusch (1), Rachel Landrum (1), Christopher A. Shera (2), Jennifer M. Groh (1)
(1) Duke University (2) University of Southern California

After every eye movement, the brain must realign the visual and auditory reference frames in order to co-locate sights and sounds. Exactly where, when, and how such visual-auditory spatial integrations occur is not fully understood. We recently discovered that the eardrum oscillates beginning a few milliseconds before saccades and continuing until well into ensuing periods of fixation (Gruters, Murphy et al PNAS 2018). Information about at least the horizontal direction and length of saccades appear to be reflected in the phase and magnitude of these eye movement-related eardrum oscillations (EMREO). Here, we sought to assess the full spatial characteristics of this signal for saccade parameters in both vertical and horizontal dimensions. Concurrently we sought to validate that independent estimations of vertical and horizontal saccade parameter contributions can be linearly combined to predict EMREO waveforms for saccades in all directions – a fundamental assumption of current analyses. We found that EMREOs depend on both horizontal and vertical saccade components, varying predominantly with eye displacement, but modulated by absolute (initial or final) position as well. In toto, EMREO appear to represent combinations of these saccade parameters such that any saccade corresponds to a specific eardrum oscillation that contains a linear combination of the vertical and horizontal saccade parameters. Regressions in both the time and frequency domain create a fuller picture of the spatial information contained in EMREO. These results demonstrate that detailed information about the relationship between visual and auditory reference frames is present in the earliest stage of the auditory pathway. They also demonstrate that this information is mapped linearly and can therefore be recovered with a small set of basis components. Future work delving into the relationship between EMREO and the transduction of incoming sounds will be needed to ascertain their effects on the processing of auditory spatial locations in relation to the visual scene. While the frequency and magnitude of EMREO suggest that they may be related to middle ear muscle contractions, the underlying mechanisms that generate them are unknown.

21 Assays of Temporal Coding in the Ascending Human Auditory Pathway

Agudemu Borjigin (1) Hari M. Bharadwaj (1) (2)"
(1) Weldon school of biomedical engineering, Purdue University
(2) Speech, language, and hearing sciences, Purdue University

Neural phase-locking to the temporal fluctuations of sound is a fundamental and unique mechanism by which sensory information is captured by the auditory periphery. However, the role of this metabolically expensive mechanism, in particular the utility of neural coding of the temporal fine structure (TFS) in everyday hearing, is debated. To address this question, our long-term strategy is to compare individual differences in TFS sensitivity to suprathreshold listening performance in tasks that represent aspects of everyday listening conditions. The focus of this presentation is our attempt to obtain robust individual-level measures of TFS sensitivity by exploring an array of both behavioral and electroencephalography (EEG)-based candidate measures in a large cohort of normal-hearing listeners. Individuals differed widely in both behavioral and passive EEG measures of the TFS sensitivity. Listeners with poor cortical (EEG-based) sensitivity to binaural interaural time differences (ITD) had poor performance in behavioral ITD detection tasks. Those listeners also had high monaural frequency modulation (FM) detection thresholds. However, the two behavior measures turned out to be uncorrelated after individual "non-sensory" scores from catch trials were factored out from each measurement pointing to the dominant role of non-sensory factors such as attention in behavioral task performance. In addition, unlike the ITD detection threshold measurement, the residual monaural FM detection thresholds did not correlate with any EEG features, indicating that monaural FM detection might be a poor assay of TFS sensitivity. In the end, cortical sensitivity to TFS combined with the "non-sensory" scores could well predict the actual behavioral ITD thresholds, accounting for more than half of the variance observed. These results underscore the importance of passive electrophysiological measures in capturing individual differences in the neural coding of TFS and hence in the clinical diagnosis of the temporal processing disorders.

22 Computational model of complex combinatorial binding: Neurobiological simulations and hypotheses

Ryan M. Calmus (1), Benjamin Wilson (1), Yukiko Kikuchi (1), Zsuzsanna Kocsis (2, 1), Hiroto Kawasaki (2), Timothy D. Griffiths (1), Matthew A. Howard, III (2), Christopher I. Petkov (1)
(1) Institute of Neuroscience, Newcastle University
(2) Department of Neurosurgery, University of Iowa

Understanding how the brain segregates and binds complex information distributed in time is a challenging endeavour for the auditory community, requiring computationally and neurobiologically informed approaches to solve. Human spoken language is a salient example of the complexity of the binding problem, since hierarchically organized dependencies (for example, nested dependencies between words and phrases in sentences) feature prominently. However, the problem is not unique to language nor humans, since complex binding in the time domain is relevant for auditory cognition more generally and for executing complex action sequences. Structured sequence learning tasks suggest roles for a broad auditory network of fronto-temporal regions including the hippocampus. However, the transformations occurring between these brain regions remain unknown, as do the neural mechanisms segmenting auditory input, detecting dependencies between discrete elements and binding elements into structured representations. We propose a blueprint for a computational model of complex combinatorial binding (entitled: Vector-symbolic Binding INstantiating Dependencies, or V-BIND). This model integrates formally defined Vector Symbolic additive and conjunctive binding operators with neurobiologically plausible dynamics, and is compatible with modern Spiking Neural Network simulation methods. The model is designed to support the binding of serially-ordered elements in structured sensory (or semantically meaningful) sequences into structured representations of dependencies; readily operates on multiple timescales; and encodes or decodes sequences with respect to chunked items wherever dependencies occur in time. We show that the model is capable of simulating previous findings under auditory structured sequence learning tasks that engage fronto-temporal regions, specifying mechanistic roles for prefrontal areas 44/45 and the frontal operculum during interactions with sensory representations in temporal cortex. Finally, we are able to make predictions based on the configuration of the model alone that underscore the importance of serial position information, which requires input from time-sensitive neurons, known to reside in the hippocampus and dorsolateral prefrontal cortex. Simulations are being tested with neurophysiological data from human intracranial recordings during surgical monitoring periods as they participate in sequence learning tasks.

23 Direct mapping of the cortical tinnitus network

Phillip E. Gander (1) William Sedley (2) Sukhbinder Kumar (2) Hiroyuki Oya (1) Christopher K. Kovach (1) Kirill V. Nourski (1) Hiroto Kawasaki (1) Matthew A. Howard III (1) Timothy D. Griffiths (2)
(1) University of Iowa
(2) Newcastle University

Tinnitus occurs when peripheral hearing damage leads to secondary changes in ongoing brain activity. These central mechanisms are poorly-understood, partly because relevant experimental evidence is almost entirely indirect, meaning it does not reflect the real-time perception of tinnitus, and/or it does not provide a direct measure of neural activity. Previously we reported on a test of this hypothesis in a human neurosurgical subject, who had an extensive array of electrocorticography and depth electrodes placed for the localization of epilepsy. Tinnitus loudness was modulated with residual inhibition using noise, and quantified with real-time ratings. Here we report an experimental replication in a second neurosurgical subject with broadly comparable tinnitus and intracranial recording. Similar findings in both subjects were obtained: 1) Suppression of tinnitus correlated with widespread reductions in delta (1-4 Hz) oscillatory power throughout most of auditory cortex, and large parts of non-auditory cortex in temporal, parietal, limbic and motor areas. These areas also showed changes in inter-regional delta phase coherence with tinnitus suppression. 2) Theta (4-8 Hz), alpha (8-12 Hz), and high beta (20-28 Hz) power was similarly suppressed in most of these areas. 3) Gamma (28-144 Hz) power increased, during tinnitus suppression, throughout auditory cortex and in posterior temporal, inferior parietal, sensorimotor and parahippocampal cortex. In the second subject electrical stimulation of Heschl's gyrus elicited reductions in tinnitus loudness comparable to that induced by sound. The change in tinnitus perception from stimulation occurred without alteration to other external auditory perception.
These findings support the definition of the brain networks critically involved in tinnitus perception which will be necessary to create effective treatments and possible cures.

24 Neural correlates of auditory stream segregation in the auditory pathways of macaque monkeys

Taku Banno (1), Jaejin Lee (1), Yonatan I. Fishman (2), Yale E. Cohen(1)
(1) University of Pennsylvania
(2) Albert Einstein College of Medicine

A fundamental component of auditory scene analysis is grouping acoustic features from different sound sources into segregated representations of auditory objects. This process is a fundamental aspect of hearing and speech perception. Although psychoacoustic studies have shown that differences in the frequency and location of sound sources provide important cues for the perceptual segregation of auditory streams in humans, the neuronal mechanisms underlying stream segregation based on these cues remain to be fully elucidated.

Here, we trained macaque monkeys to report a deviantly loud target stimulus that was embedded in one of two temporal sequences of tone bursts; each tone burst, except a "target" tone burst had a random sound level. In humans, the detection of this target stimulus was harder when the frequency difference between the tone-burst sequences was small and became easier as the frequency difference increased. Similarly, detection became easier when the angular separation increased and harder when this separation decreased. Importantly, because the target can only be reliably detected when the two tone sequences are perceptually segregated, this stimulus paradigm provides an objective measure of auditory streaming. As in the human studies, we found that the monkeys' performance improved as the frequency difference or the angular separation of the tone-burst sequences became larger, suggesting the monkeys utilize frequency and location cues in a similar way to humans in auditory streaming.

While a monkey participated in the target detection task, we recorded neuronal activity in the primary or nonprimary auditory cortex. We set the best frequency of the recorded neurons to be that of the tone-burst sequence that contained the target stimulus. We found that, in the primary auditory cortex (A1), neurons responded to each presentation of the tone bursts with the response magnitude reflecting the frequency tuning of the neurons. In contrast, neurons in the lateral belt showed sustained activity throughout the trial and the magnitude of the responses to the low- and high-frequency tone bursts was not clearly distinct, even though lateral-belt neurons had frequency tuning as sharp as those in A1. To our knowledge, this is the first study to compare neuronal responses in primary and nonprimary auditory cortex that may be relevant for auditory streaming in non-human primates. Our behavioral and physiological results suggest that this stimulus paradigm provides a promising tool for elucidating neural mechanisms contributing to auditory scene analysis.

25 Differing release patterns of dopamine and acetylcholine in the mouse basolateral amygdala in response to high-arousal vocal sequences

Zahra Ghasemahmad (1,2), Jeffrey Wenstrup (1,2)
(1) Northeast Ohio Medical University
(2) Kent State University

Social vocalizations, reflecting the internal state of a sender, can change the internal state and behavior of listeners. These listener responses are mediated, in part by the basolateral amygdala (BLA), an emotional brain center shaping reactions to salient and valent stimuli and are thought to depend on inputs from neuromodulatory centers. Here, we examine how emotion-laden vocalizations evoke patterns of neurochemical release within the mouse BLA. A liquid chromatography/mass spectrometry (LC/MS) technique allowed simultaneous detection of non-electroactive chemicals (GABA and acetylcholine (ACh)) and catecholamines in the same samples. For playback of highly emotion-laden vocalizations of CBA/CaJ mice, we identified vocal sequences that were characteristic of restraint (aversive) and an intense stage of mating (appetitive). We presented 5 exemplars from each context. Mice were tested in 3 groups: males-mating, males-restraint, and females-mating (w/estrous monitoring). These groups were chosen based on previous results showing sexually dimorphic reactions to mating vocalizations but similar behavioral responses to restraint calls. After experiencing mating and restraint situations in a counterbalanced order on consecutive days, mice were implanted with a microdialysis probe and CSF samples were collected from BLA before, during, and after vocalization playback in 10-min intervals. Probe location in or adjacent to BLA was histologically confirmed. Samples were analyzed using LC/MS and concentrations of neurochemicals were monitored and correlated with behavior. Here we report on the release of ACh and dopamine (DA). During 20-min playback of mating vocalizations, DA increased in both male and female mice and remained elevated after playback for 1 hour. However, ACh concentration decreased during playback and returned to baseline after the mating vocalizations stopped. In contrast, playback of restraint vocalizations decreased DA during and after playback of the vocalizations, while ACh showed a transient increase in concentration during playback and returned to baseline after playback stopped. Our findings suggest interplay between ACh and DA release in the BLA may contribute to distinct behavioral responses to appetitive and aversive vocal sequences.

26 Alpha and gamma power in medial prefrontal cortex reinforces reward contingencies and predicts asymptotic performance in a cognitive flexibility task

Howard Gritton (1), Nicholas M. James (1), Jian Carlo Nocon (1), Moona Abdulkerim (1), Kamal Sen (1), Xue Han (1)
(1) Boston University

The ability to adapt to ever-changing environments represents a key tenet of cognitive function and executive control. Fundamental to this process is the integration of sensory cues, decision making and the executive control of behavior. The processes by which cortical circuits are modified by changes in task rules are not completely understood, but could involve changes in prefrontal regions that are ultimately conveyed to sensory regions important for stimulus monitoring. To understand the functional role of cognitive flexibility, and how changes in task rules influence frontal and sensory regions, we recorded from auditory (AC) and medial prefrontal cortex (mPFC) while mice performed an auditory extinction learning task. Prior to recording, animals were trained to lick for a small water reward that had been paired with two distinct tones separated by 1.5 octaves. Once the associations were well learned, recordings were made from animals when the reward was withdrawn from one of the two tones while the other was maintained. We found the change in task rules produced immediate and robust changes in both higher gamma (50-75 Hz) and alpha (8-12 Hz) power during a confusion interval that occurred prior to animals learning to modify their behavior. The changes in gamma and alpha were unique to different trial types and their augmentation differed in relationship to the reward window. Gamma was enhanced during reward intervals only for still rewarded tones. In contrast, alpha power rose at the conclusion of the reward window and only following the extinguished tone. This increase in power was observed in mPFC before AC, suggesting that mPFC is recruited earlier in extinction learning than AC. Furthermore, the strength of alpha power in the mPFC was also strongly predictive of the asymptotic performance the animal would later achieve in the training session. We found that both changes in gamma and alpha power persisted even as performance improved, suggesting these rhythms may have an ongoing role in the maintenance of newly learned associations, or represent components of expected value under the new outcome contingencies.

27 Behavioral and neural evidence for implicit memory for regularities in rapid sound sequences

R. BIANCO(1), C. BOLGER(1), M. HU(1), P. HARRISON(2), M. PEARCE(2), M. CHAIT(1);
(1)UCL, London, United Kingdom;
(2)Queen Mary Univ., London, United Kingdom

Sensitivity to acoustic statistical regularities is fundamental to many aspects of auditory perception and cognition. Recent work using repeated noise paradigms demonstrated robust, long-term auditory implicit memory for 'frozen' reoccurring white noise. Participant performance suggested that they become sensitive to an idiosyncratic, local spectral feature within the noise samples. Here we focus on implicit memory for sequences of auditory events - a specific arrangement of twenty different 50ms tone pips. Using behavioural methods, modelling and EEG in humans we ask (1) whether listeners can remember complex sequences of acoustic events (2) the limits on this memory (3) whether it requires active involvement with the sequence.
Building on previous work from our lab (Barascud et al, 2016), participants monitored novel rapid sequences of tone-pips for a transition from a random to a regular frequency pattern (repeating cycles of twenty 50 ms tone-pips). On half of the trials, sequences were random throughout; the other half contained a transition from a random to a regularly repeating pattern at a random time partway through the sequence. Most of the regular patterns were generated anew for each trial. Unbeknownst to the participants, several regular patterns (different for each listener) sparsely reoccurred across trials (every ~2.5 minutes) .
Compared with novel sequences, response time (RT) to reoccurring regularities became substantially faster within only a few reoccurrences, reflecting rapid learning of sequence structure. This benefit persisted after 24 hours, and up to 7 weeks; it was robust to doubling the number of regularities to memorise, and to subsequent memorization of other patterns. Similar learning also occurred during passive exposure (i.e when naive listeners were listening passively, without performing a transition detection task).
Overall, we show that as regularities reoccur they are implicitly stored in memory, progressively up-weighted and more quickly retrieved to resolve the identity of sensory signals. EEG measurements from passively listening participants exposed to recurring patterns are also provided to demonstrate a progressive change in brain responses with sequence structure learning.
Barascud, N., Pearce, M.T., Griffiths, T.D., Friston, K.J, Chait, M (2016). Brain responses in humans reveal ideal observer-like sensitivity to complex acoustic patterns. PNAS 113 (5), E616-E625. doi:10.1073/pnas.1508523113

28 Tracking of 1/f stimulus characteristics in the human EEG

Leonhard Waschke (1,2), Thomas Donoghue (2), Sydney Smith (2), Bradley Voytek (2), Jonas Obleser (1)
(1) Department of Psychology, University of Lübeck
(2) Department of Cognitive Science, University of California San Diego

The statistics of both human electrophysiology data and many natural stimuli follow a power law, that is, they share a 1/f^chi distribution. Both kinds of time series hence are characterized by pronounced events that occur with relatively low frequency compared to more subtle fluctuations arising with higher frequency. This reduction in signal magnitude with increasing frequency is aptly captured by the slope, or exponent (chi) of the power spectral density (PSD).

Recently, the spectral exponent of electrophysiological recordings has been suggested as a marker of inter-individual traits and behaviourally relevant brain states. Specifically, the spectral exponent captures aperiodic, non-oscillatory parts of electrophysiological signals and has been hypothesized to reflect the balance of excitatory and inhibitory activity (E:I ratio) in populations of cortical neurons. It is unclear, however, to which degree bottom-up influences like stimulus characteristics alter the electrophysiological spectral exponent. Additionally, the impact of top-down processes such as the selective allocation of cognitive resources on the PSD and its interplay with sensory factors is unknown.

We here present evidence from two different experiments, during which we recorded electroencephalography (EEG) while participants (total N = 44) detected faint target stimuli in streams of auditory or visual noise. Importantly, all noise stimuli were generated to exhibit different 1/f chi values (0, 1, 2, 3) in their modulation spectra.

Spectral exponents over auditory and visual sensory cortices were positively related to chi values of the respective stimulus domain, and thus tracked stimulus characteristics on the single-trial level. Notably, conventional metrics of EEG analysis such as event related potentials were insensitive to these changes. The tracking of stimulus statistics did not hinge on modality-specific attention. However, we find that modality-specific attention reduced spectral exponents, i.e. caused a flattening of EEG spectra. Within the E:I framework, this would relate to an increased E:I ratio (E>I) over sensory regions of the attended domain. These results demonstrate the importance of aperiodic, non-oscillatory component of electrophysiological signals, captured by the spectral exponent, for the study of sensory and cognitive functions. We relate our results with the tracking of stimulus information in the time domain using temporal response functions and discuss the relevance of tracking stimulus statistics for behaviour.

29 The auditory dorsal pathway mirrors the semantic hierarchy of speech prediction

Lea-Maria Schmitt (1), Julia Erb (1), Sarah Tune (1), Anna Rysop (2), Gesa Hartwigsen (2), Jonas Obleser (1)
(1) Department of Psychology, University of Lübeck, Germany
(2) Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

When poor acoustics challenge speech comprehension, listeners are thought to increasingly draw on semantic context to predict upcoming speech. However, previous research focused mostly on predictions derived from isolated speech material with short timescales of context (e.g., sentences). We here ask how the human brain builds up predictions when confronted with a multitude of timescales characteristic of natural speech. In a 3-T fMRI study, healthy participants (N=60, 18–74 years) listened to a one-hour natural narrative embedded in a competing stream (0 dB SNR) of resynthesized natural sounds. To model semantic predictability at five timescales corresponding to a logarithmic increase in context length (i.e., 1–24 content words), we computed the similarity between the word2vec embedding of each content word in the story and each timescale's average word embedding. In an initial analysis of data from 30 younger participants, we mapped the timescales of semantic predictability onto the BOLD signal using voxel-wise ridge regression within a fourfold cross-validation scheme. We found that the timescales of semantic prediction are organized along an auditory dorsal processing hierarchy: increased activity in the posterior portion of superior temporal gyrus is tightly coupled to short informative timescales, whereas parietal regions like the temporo-parietal junction and angular gyrus are most responsive to long informative timescales. Furthermore, brain areas most responsive to long timescales largely overlap with the dorsal default mode network. Next, we will use a measure of semantic predictability fine-tuned to the unique hierarchical structure underlying the context of each word by incorporating a deep neural network trained to determine the probability of an upcoming word given the semantics of a timescale.

30 Temporal context invariance reveals neural processing timescales in human auditory cortex

Sam V Norman-Haignere (1,2), Laura K. Long (1,3), Orrin Devinsky (4,5), Werner Doyle (5,6), Guy M. McKhann (7), Catherine A. Schevon (7), Adeen Flinker (4,5), Nima Mesgarani (1,3,8)

1. Zuckerman Institute for Brain Research, Columbia University
2. HHMI Postdoctoral Fellow of the Life Sciences Research Foundation
3. Program in Neurobiology and Behavior, Columbia University
4. Department of Neurology, NYU Langone Medical Center
5. Comprehensive Epilepsy Center, NYU Langone Medical Center
6. Department of Neurosurgery, NYU Langone Medical Center
7. Department of Neurology, Columbia University Medical Center
8. Department of Electrical Engineering, Columbia University

Natural sounds like speech and music are structured at many timescales, but it remains unclear how these diverse timescales are cortically represented. Do processing timescales increase along the putative cortical hierarchy? What timescales are used to code speech and music? Is there hemispheric or anatomical specialization for processing particular timescales? Answering these questions has been challenging because there is no general method for estimating integration periods: the time window within which stimulus features alter the neural response. Here, we introduce a simple experimental paradigm (the "temporal context invariance" paradigm) for inferring the integration period of any sensory response. We present sequences of natural sound segments in which the same segment occurs in two different contexts (different surrounding segments), and test how long the segments need to be for the response to become context invariant. By applying this paradigm to intracranial recordings from epilepsy patients (broadband gamma power), we map neural processing throughout human auditory cortex. This map reveals a four-fold increase in timescales between primary (~100 ms) and non-primary regions (~400 ms). Using a separate dataset of responses to a diverse set of natural sounds, we then test what information can be decoded from populations of electrodes with different integration periods. We find that spectral information is best decoded from short integration period electrodes (<200 ms) while sound categories (speech & music) are best decoded at longer timescales (>200 ms). These results provide support for hierarchical models, demonstrate the timescale at which speech and music selectivity first emerge, and validate our method.

31 Chronic Bilateral Stimulation through Cochlear Implants during Development Can Reverse the Effect of Early-Onset Deafness on Neural ITD Sensitivity

Woongsang Sunwoo (1,2,3), Bertrand Delgutte (1,2), Yoojin Chung (1,2)
(1) Eaton-Peabody Laboratories, Massachusetts Eye & Ear, Boston, Massachusetts, 02114, USA
(2) Department of Otolaryngology-Head and Neck Surgery, Harvard Medical School, Boston, Massachusetts, 02115, USA
(3) Department of Otolaryngology, Gachon University Gil Medical Center, Incheon, 405-760, South Korea

Bilateral cochlear implant (CI) users with a pre-lingual onset of hearing loss show poor sensitivity to interaural time differences (ITD) compared to those with post-lingual hearing loss. Similarly, neural ITD sensitivity in the inferior colliculus (IC) of rabbits that are deafened as neonates is degraded compared to animals deafened as adults. Here we investigated whether chronic bilateral CI stimulation during development can reverse the effect of early-onset deafness on ITD sensitivity.
Four Dutch-belted rabbits were deafened as neonates with daily injection of neomycin and then bilaterally implanted at 2 months of age. Starting just after implantation, they received daily stimulation (5 hrs/day) by environmental sounds using wearable sound processors programmed with the "Fundamental Asynchronous Stimulus Timing" (FAST) strategy designed to deliver ITD information effectively with bilateral CIs. Single-unit recording from the IC using an unanesthetized preparation commenced at 5 months of age. Stimuli were periodic trains of biphasic electric pulses with varying pulse rates (20 – 640 pps) and ITDs (-2000 to +2000 μs). The results are compared to measurements from adult-deafened rabbits (Chung et al., J Neurosci. 36:5520) and early-deafened rabbits that did not receive daily stimulation (Chung et al. JARO. 20:37).
More IC neurons in the stimulated rabbits showed significant ITD sensitivity in their overall firing rate (75%) compared to unstimulated animals (62%). The difference in prevalence of ITD sensitivity was most prominent at high pulse rates (>200 pps). ITD sensitivity based on analysis of variance and neural ITD discrimination thresholds also showed improvements in the stimulated animals compared to unstimulated animals, with the largest effect found at high pulse rates. The fraction of ITD sensitive neurons, and ITD STVRs and thresholds in the stimulated animals were comparable to those from adult-deafened animals at high pulse rates.
In summary, chronic bilateral cochlear implant stimulation during development can partly reverse the degradation in neural ITD sensitivity resulting from early-onset deafness. The effect is most pronounced in response to high-rate stimulation."

32 Metamers of audio-trained deep neural networks

Jenelle Feather (1), Alex Durango (1), Ray Gonzalez (1), Josh McDermott (1,2)
(1) Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology
(2) Program in Speech and Hearing Bioscience and Technology, Harvard University

Deep neural networks have been embraced as models of sensory systems, instantiating representational transformations that appear to resemble those in both the visual and auditory systems. To more thoroughly investigate the similarity of artificial neural networks to biological systems, we synthesized model metamers – stimuli that produce the same responses at some stage of a network's representation – and asked whether they also produce similar responses in the human auditory system. We generated model metamers for natural speech by performing gradient descent on a noise signal, modifying the noise signal so as to match the responses of individual neural network layers to the responses elicited by a speech signal. We then measured whether model metamers were recognizable to human observers – a necessary condition for the model representations to replicate those of humans. Although model metamers from early network layers were recognizable to humans, those from deeper layers generally were not, indicating that the invariances instantiated in the network diverged from those of human perception. However, the model metamers became more recognizable after architectural modifications that might be expected to yield better models of a sensory system (by reducing aliasing artifacts from downsampling operations). Moreover, metamers were more recognizable for networks trained to recognize speech than those trained to classify auditory scenes, suggesting that model representations can be pushed closer to human perception with appropriate training tasks. Our results reveal discrepancies between model and human representations, but also show how metamers can elucidate model representations and guide model refinement.

33 Cortical mapping of prediction error responses to multiple sensory features

HyunJung Ahn(1), Ryszard Auksztulewicz(1,2) , Jan W. Schnupp(1)
(1) Department of Biomedical Science City University of Hong Kong, Hong Kong
(2) Department of Neuroscience, Max Planck Institute for Empirical Aesthetics, Frankfurt, Germany

Predictive coding is widely accepted as a comprehensive theory of neural processing underlying perceptual inference. However, it is unknown to what extent prediction violations of different sensory features are mediated in different regions in auditory cortex, with different dynamics and by different mechanisms. This study investigated the neural responses to synthesized acoustic syllables which could be expected or unexpected along several features. By using electrocorticography (ECoG) in rat auditory cortex, we mapped regional differences in mismatch responses to different stimulus features.
The subjects were 8 adults female Wistar rats (age range: 8-20 weeks) with normal hearing and no prior exposure to the stimuli. Morphed syllables formed roving oddball sequences in which each stimulus was repeated 2-43 times (thereby forming a standard) with the inter-stimulus interval fixed at 300ms, and subsequently replaced with a deviant stimulus, differing from the standard along one of several acoustic features (duration, pitch, interaural level differences (ILD) and consonant identity). Each of these features could assume one of 9 different levels (durations: 55-95ms in 5ms steps ; pitch mean F0: 0.7-1.4kHz logarithmically spaced; ILD : 60-68 dB SPL difference in 2 dB steps; consonant: /da/-/ba/ in equidistant steps), and the resulting deviance magnitude ranges between +4 and -4 steps. The deviant stimuli were then repeated to form new standards. We analyzed responses to the last repetition of a given stimulus (standard) and the first repetitions of a new stimulus (deviant). For the ECoG recording, we implanted urethane-anaesthetised rats with 8x8 electrode arrays covering a 3x3mm cortical patch encompassing primary and higher-order auditory cortex. In each rat, we presented a total 3800 stimuli, amounting to ~40 deviant stimuli (and their preceding standards) for each feature and level of deviance magnitude.
We identified different the topographies and latencies of population activity in the rat auditory regions sensitive to expectation violation along different acoustic features. Responses to deviant stimuli increased in amplitude with increasing deviance magnitude. Mismatch response to both duration and ILD violations were observed in anterior auditory regions but at slightly earlier latencies for duration vs. ILD violations. In contrast, mismatch response to pitch and consonant identity were observed at posterior and dorsal electrodes, with consonant violations evoking earlier mismatch responses than pitch violations. This suggests differences in cortical regions and populations dynamics subserving prediction error signaling along different stimulus features."

34 Temporal weighting functions for binaural cues in rats

Kongyan Li(1), Chloe H. K. Chan(1), Ambika Prasad Mishra(1), Jan W. H. Schnupp(1,2)

(1) Department of Biomedical Sciences, City University of Hong Kong, 31 To Yuen Street, Kowloon Tong, Hong Kong
(2) City University of Hong Kong Shenzhen Research Institute, Shenzhen, China 518057

The “temporal weighting function” (TWF) quantifies how strongly lateralisation judgments in spatial hearing are influenced by the onset, middle, or offset of a sound respectively. They are usually measured in psychoacoustic experiments using binaural click trains, in which individual clicks differ in their binaural cue values. Human listeners tend to show a strong “onset bias” in such studies (Brown and Stecker, 2010; Stecker and Hafter, 2002; Stecker, 2014). While the shape of the TWF is likely to be similar in other mammals, to the best of our knowledge, this has not previously been shown. To measure the TWF for rats, we performed psychoacoustic experiment using click train stimuli with jittered interaural time differences (ITDs). Four 8-week old female Wistar rats performed a two-alternative forced choice near-field lateralization task. The experiments involved randomly interleaved “honesty trials” (80% of trials), and “probe trials” (20%). We then computed TWFs by performing a multiple regression of the ITD value against the animals’ “left” or “right” responses for the probe trials only. ITD TWFs were measured in this way for click rates of 20, 50, 300 and 900 Hz. Onset dominance was observed across all click rates for all rats. The weights on the later clicks tended to increase as the click rate decreased. In a few cases, significant weight on the last click (offset) was also found, mainly in the lower frequencies. Our findings demonstrated that the auditory process in rats is similar to human, showing clear onset dominance and recency effect. The rat is therefore shown to be an easily accessible and feasible animal model for related auditory research.

35 Anterior temporal lobe disconnection disrupts neural responses to speech along the human auditory cortical neural network

Z. KOCSIS (1,2), R. L. JENISON (3), B. MCMURRAY (4), A. E. RHONE (1), M. E. SARRETT (4), P. E. GANDER (1), K. V. NOURSKI (1), M. STEINSCHNEIDER (5), R. M. CALMUS (2), H. KAWASAKI (1), J. D. GREENLEE (1), C. K. KOVACH (1), T. D. GRIFFITHS (2), M. A. HOWARD, III (1), C. I. PETKOV (2)
(1) Department of Neurosurgery, University of Iowa, Iowa City, IA, USA
(2) Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK
(3) Departments of Neuroscience and Psychology, University of Wisconsin, Madison, WI, USA
(4) Department of Psychological and Brain Sciences, University of Iowa, Iowa City, IA, USA
(5) Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, USA

Understanding the impact of surgical disconnection on neural responses in the human brain has the potential to advance models of normal neurophysiology and its disruption by pathology. We present data from five patients who underwent surgical disconnection of the anterior temporal lobe (ATL) as part of their clinical procedure to treat intractable epilepsy. In three patients, we obtained intraoperative electrocorticographic (ECoG) recordings pre- and post-resection while the patient was lightly sedated, but awake and responsive during a speech-sound perceptual prediction task. In two of the patients, we were also able to obtain pre- and post-operative magnetic resonance imaging (MRI) including T1 and T2 structural and diffusion-weighted scans. Time-frequency analyses of data recorded from auditory cortex (Heschl's gyrus and superior temporal gyrus, STG) demonstrated an enhancement of the high-gamma response to speech sounds post disconnection. Moreover, as a result of ATL disconnection, we observed changes in the timing and magnitude of the neurophysiological signal at lower frequencies, notably beta, in auditory cortex and other sites (such as STG and inferior frontal cortex). These results show disruption of the broader auditory processing network and are interpreted within the context of predictive coding theory. Post-operative T1- and T2-weighted structural MRI scans were used to identify the surgical lesion. Probabilistic diffusion tensor imaging (DTI) tractography using seeds in the anterior temporal lobe confirmed disconnection of the temporal pole from areas caudal to the clinical resection, including auditory cortex. Disruption of functional connectivity between disconnected and intact cortex was confirmed with spectrally-resolved, state-space Granger Causality analyses of the task-based neurophysiological data, revealing changes of inter-regional connectivity within the intact cortex for specific oscillatory frequency bands. These rare datasets provide first impressions of the crucial impact on speech processing in human auditory cortex and the broader auditory neural network following anterior temporal lobe disconnection.

36 Comparison of Dendritic Spine Density/Size for Anterior Auditory Field Neurons from Early-deaf and Hearing Cats.

M. Alex Meredith (1), Stephen G Lomber (2), H. Ruth Clemo (1)
(1) Virginia Commonwealth University School of Medicine
(2) McGill University

Following early deafness, the Anterior Auditory Field (AAF) is crossmodally reorganized to exhibit visual/somatosensory activity. Unlike other auditory fields following deafness, the AAF incurs a substantial loss of inputs from other auditory cortices (Wong et al, 2015). This, and other functional differences among auditory cortical regions in deaf cats suggest that the AAF may exhibit area-specific distinctions in synaptic plasticity following deafness. The present study measured the dendritic spine features of spine density and spine head diameter from AAF neurons in early-deaf cats (D; ototoxic administration within the first post-natal month, confirmed by flat ABR) and hearing (H) controls. The AAF cortex of adult cats (D= 3; H=3) was incubated for Golgi-Cox staining. Reactive neurons identified within AAF were visualized and their dendritic spine features assessed using a light microscope (100x; oil) controlled by Neuroludica software. The overall dendritic spine density (809 dendritic segments) did not vary significantly (H=0.76 spines/µm ± 0.01 se; D=0.76 spines/µm ± 0.01 se). However, spine density significantly increased in the granular (thalamo-recipient) layers (H=0.55 spines/µm ± 0.02 se; D=0.71 spines/µm ± 0.02 se; $p<0.0001$) but was not changed in the supra- or infragranular layers. The diameter of dendritic spine heads was measured for 9011 spines, revealing that spine heads from early-deaf (D) animals were slightly but significantly larger (D avg. = 0.59 µm ± 0.002 se) than those of their hearing (H) counterparts (H avg. = 0.53 µm ± 0.002 se; $p<0.0001$), and a significant increase in spine diameter was exhibited by neurons in all layers of AAF following deafness. These data indicate that dendritic spines in AAF react to early hearing loss in a lamina-dependent manner. Following deafness, the supragranular layers of AAF incur a substantial loss of inputs from other auditory cortices (such as A1). Therefore, it is provocative that the granular, thalamo-recipient, layers of AAF actually show an increase in spine density, and that there is no change in spine density in the supragranular layers that experience a decrease in corticocortical connectivity. In total, when compared with other auditory areas following deafness, these data reaffirm the notion that cortical crossmodal plasticity employs different synaptic strategies for different regions.

37 Neural correlates of figure-ground segregation in anterolateral fields of the monkey auditory cortex

Felix Schneider (1), Fabien Balezeau (1),Yukiko Kikuchi (1), Chris Petkov (1), Alexander Thiele (1), Timothy Griffiths (1)

(1) Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, United Kingdom

Across sensory modalities, figure-ground segregation is critical for scene analysis. This is a particularly challenging problem in the auditory system where different sound objects emanating from the same spatial location have to be dynamically decoded using spectro-temporal features that are difficult to segregate from noisy backgrounds. Previous imaging studies have shown an involvement of non-primary auditory regions in both humans (Teki et al. 2011, 2016) and macaques (Schneider et al. 2018), however, the underlying neural mechanisms remain unknown. The aim of this study was to identify the neurophysiological correlates of figure-ground segregation in the auditory cortex of macaque monkeys using fMRI-guided electrophysiological recordings.

We investigated neuronal responses to stochastic figure-ground stimuli in two macaques. We recorded spiking and local field potentials (LFPs) in the auditory core and surrounding belt while the animals performed a Go/No-Go figure detection task. We show a significant increase in firing rate to auditory figures across cortical areas, with shorter response latencies in the anterior compared to the posterior recording regions. A figure modulation index revealed a comparable effect size across fields but we found a higher fraction of figure-ground responsive cells in the anterolateral auditory cortex. Generally, higher figure coherence causes earlier and larger increments in firing rate. The analysis of LFPs revealed figure-ground related changes in the beta and gamma band.

Our results indicate that this form of auditory scene analysis depends on anterolateral auditory fields and suggest that bottom-up information is first integrated in subpopulations of neurons further along the ventral processing pathway in the auditory cortical hierarchy. These neurons respond to a broad range of frequency bands and can detect temporally coherent elements devoid of simple mathematical relationships between acoustical components. Our results confirm and extend with direct neurophysiolocal evidence earlier fMRI studies (Teki et al. 2011; Schneider et al. 2018).

38 Attentional capture in budgerigars (Melopsittacus undulatus)

Huaizhen Cai (1), Micheal L. Dent (2)
University at Buffalo

Budgerigars were trained to discriminate a frequency deviant in an auditory streaming task to determine if they experience attentional capture. ABAB… patterned pure tone sequences (where the frequency separation between the A and the B tones was 8 semitones) were used as stimuli. The birds were trained to attend to the target stream consisting of A tones while ignoring the background stream consisting of B tones, by responding to a frequency deviant appearing at random sequential locations in the target stream, while withholding the response to the frequency deviant in the background stream. Across sessions, the background deviant took different values of perceptual salience. Response latencies and minimum detectable frequency deviant thresholds in the target stream were calculated as indicators of the manipulation of selective auditory attention in the auditory streaming task. Thresholds increased as the frequency deviants in the background streams became more salient. Also, shorter response latencies were observed for trials with background deviants appearing further away (sequential locations) from the target deviant, indicating that it takes time for birds to switch their selective attention from the unattended distractors to the attended targets. Hence, birds experience attentional capture in auditory streaming, even though they were trained to ignore the background. Further studies need to be conducted to elucidate the neural mechanisms of the interactions between bottom-up and top-down process in auditory selective attention.

39 Cortical tracking of words during natural story comprehension

(1)Cheng Luo, (2)Nai Ding
(1)Zhejiang University
(2)Zhejiang University

During speech comprehension, the brain decodes meaning based on the acoustic features of speech.Words are primary units of meaning and a crucial step of speech comprehension is to segment a continuous speech stream into discrete words. Finding the boundaries between words is not a trivial task, which relies on not only auditory analysis but also linguistic knowledge. Previous studies have found that, when listening to speech, low-frequency cortical activity can track multi-syllabic words even when the word boundaries are not conveyed by acoustic cues. These results suggest that the brain can apply linguistic knowledge to group syllables into multi-syllabic words. Nevertheless, these results are obtained when listening to either word lists or lists of unrelated sentences. Whether low-frequency cortical activity can track multi-syllabic words during more natural speech comprehension remains unclear. Here we constructed short stories in which all words are bisyllabic words and recorded neural responses to these stories using electroencephalography (EEG). The only task of the listeners is to answer comprehension questions after each story. We found that EEG responses of the listeners concurrently tracked both syllables and bisyllabic words. These results demonstrated that the brain groups syllables into words during natural story perception and this process is reflected by word-rate neural entrainment.

40 Eye activity tracks task-relevant structures during speech and auditory sequence perception

Peiqing Jin (1), Jiajie Zou (2), Tao Zhou (3), Nai Ding (4)
(1) Zhejiang University
(2) Zhejiang University
(3) Zhejiang University
(4) Zhejiang University

The sensory and motor systems jointly contribute to complex behaviors, but whether motor systems are involved in high-order perceptual tasks such as speech and auditory comprehension remain debated. Here, we show that ocular muscle activity is synchronized to mentally constructed sentences during speech listening, in the absence of any sentence-related visual or prosodic cue. Ocular tracking of sentences is observed in the vertical electrooculogram (EOG), whether the eyes are open or closed, and in eye blinks measured by eyetracking. Critically, the phase of sentence-tracking ocular activity is strongly modulated by temporal attention, i.e., which word in a sentence is attended. Ocular activity also tracks high-level structures in non-linguistic auditory and visual sequences, and captures rapid fluctuations in temporal attention. Ocular tracking of non-visual rhythms possibly reflects global neural entrainment to task-relevant temporal structures across sensory and motor areas, which could serve to implement temporal attention and coordinate cortical networks.

41 Auditory and language contributions to neural encoding of speech features in noisy environments

Jiajie Zou (1), Jun Feng (2), Tianyong Xu (3), Peiqing Jin (4), Cheng Luo (5), Jianfeng Zhang (6), Xunyi Pan (7), Feiyan Chen (8), Jing Zheng (9), Nai Ding (10)
(1) Zhejiang University
(2) Hangzhou Normal University
(3) Zhejiang University
(4) Zhejiang University
(5) Zhejiang University
(6) Zhejiang University
(7) Zhejiang University
(8) Zhejiang University
(9) Zhejiang University
(10) Zhejiang University

Recognizing speech in noisy environments is a challenging task that involves both auditory and language mechanisms. Previous studies have demonstrated human auditory cortex can reliably track the temporal envelope of speech in noisy environments, which provides a plausible neural basis for noise-robust speech recognition. The current study aimed at teasing apart auditory and language contributions to noise-robust envelope tracking by comparing the neural responses of 2 groups of listeners, i.e., native listeners and foreign listeners who did not understand the testing language. In the experiment, speech signals were mixed with spectrally matched stationary noise at 4 intensity levels and listeners' neural responses were recorded using electroencephalography (EEG). When the noise intensity increased, the neural response gain increased in both groups of listeners, demonstrating auditory gain control. Language comprehension generally reduced the response gain and envelope-tracking precision, and modulated the spatial and temporal profile of envelope-tracking activity. Based on the spatio-temporal dynamics of envelope-tracking activity, a linear classifier can jointly decode the 2 listener groups and 4 levels of noise intensity. Altogether, the results showed that without feedback from language processing, auditory mechanisms such as gain control can lead to a noise-robust speech representation. High-level language processing modulated the spatio-temporal profile of the neural representation of speech envelope, instead of generally enhancing the envelope representation.

42 Acoustic Trauma Following Blast-Induced Traumatic Brain Injury (TBI) in CBA/CaJ Mice

Kali Burke(1), Senthilvelan Manohar (2), Richard J. Salvi (2), Micheal L. Dent (1)
(1) Department of Psychology University at Buffalo, SUNY
(2) Department of Communicative Disorders and Sciences University at Buffalo, SUNY

Exposure to a high intensity blast from the detonation of improvised explosive devices (IEDs) can lead to a traumatic brain injury (TBI) and concurrent trauma to major auditory structures. Research on whether this trauma is permanent or temporary has been inconclusive due to heterogeneity of injury acquisition. A blast wave system that generates consistent and controllable blast waves has been developed, allowing for investigation into the co-morbidity of auditory damage and TBI. In the current study, the effects of blast exposure on auditory brainstem responses (ABRs) and distortion product otoacoustic emissions (DPOAEs) in male and female mice were measured. ABRs and DPOAEs were collected prior to exposure to a blast to represent the baseline auditory capacity of each individual subject. Mice were then tested at 3, 30, and 90 days after the exposure to capture initial trauma and the degree of recovery. Shifts in ABR and DPOAE thresholds were observed in post-exposure mice, indicating trauma to central and peripheral auditory systems. Following the 90-day tests, brains and cochleae were collected and stained to examine potential inner and outer hair cell loss and degeneration. Supported by R01DC016641 to MD and SU-19-01 to KB.

43 Cortical responses to auditory novelty across task conditions as revealed by intracranial recordings

Kirill Nourski (1), Mitchell Steinschneider (2), Ariane Rhone (1), Hiroto Kawasaki (1), Matthew Howard (1) Matthew Banks (3)
(1) The University of Iowa
(2) Albert Einstein College of Medicine
(3) University of Wisconsin - Madison

Elucidating changes in predictive coding across attentional and arousal states is a major focus in neuroscience. The local/global deviant paradigm (Bekinschtein et al, PNAS 2009 106:1672-7) engages auditory predictive coding over short (local deviance, LD) and long (global deviance, GD) time scales, and has been used to assay disruption of auditory predictive coding upon loss of consciousness. Previous work (Nourski et al, J Neurosci 2018 38:8441-52) has examined effects of propofol anesthesia on short- and long-term novelty detection. GD effects were suppressed at subhypnotic doses of propofol, suggesting that they may be more related to attention than consciousness per se. The present study addressed this hypothesis by comparing cortical responses to auditory novelty between passive and active task conditions in awake listeners.
Subjects were adult neurosurgical patients undergoing chronic invasive monitoring for medically intractable epilepsy. Sequences of five 100 ms vowels separated by 50 ms silent intervals were presented to subjects as they watched a silent TV program and attended to its content (passive task) or pressed a button in response to GD target stimuli (active task). Intracranial recordings were made from core and non-core auditory, temporo-parietal auditory-related, prefrontal and sensorimotor cortex. Task performance was measured as sensitivity index, hit rate and reaction times. Cortical activity was measured as averaged auditory evoked potentials (AEPs) and high gamma (70-150 Hz) event-related band power. The onset of the stimuli and LD elicited robust AEPs in all studied brain areas in both passive and active experiments. The active task was associated with an increase in the fraction of sites with AEPs to stimulus onset and the LD effect in prefrontal cortex. High gamma responses to stimulus onset and LD were localized predominantly to the auditory cortex in the superior temporal plane and had a comparable spatial extent between the two conditions. In contrast, GD effects were greatly enhanced during the active task in auditory cortex on the lateral superior temporal gyrus, auditory-related, prefrontal and sensorimotor cortex. The prominence of GD effects was associated with individual subjects' task performance.
The data demonstrate distinct attention-related effects on responses to auditory novelty across the cortical processing hierarchy. The results motivate closer examination of effective connectivity underlying attentional modulation of cortical sensory responses, and serve as a foundation for examining changes in sensory processing associated with general anesthesia, sleep and disorders of consciousness.

44 Direct comparison of nonlinear sensory encoding models in ferret primary auditory cortex

Jacob Pennington (1,2), Stephen David (2)
(1) Washington State University Vancouver
(2) Oregon Health & Science University

A common framework for describing the function of auditory neurons is the linear-nonlinear spectro-temporal receptive field (LN STRF). This model casts a neuron's sound-evoked activity at each moment in time as the linear weighted sum of the immediately preceding sound spectrogram, followed by nonlinear rectification. However, the LN STRF is an incomplete model since it cannot account for context-dependent encoding or other nonlinear aspects of auditory processing. Two alternative models have improved on the predictive power of the LN STRF by accounting for experimentally observed biological mechanisms: short-term plasticity (STP) and contrast-dependent gain control (GC). While both models improve performance over the LN model, they have never been compared directly. Thus, it is unclear whether they account for separate processes or simply describe the same phenomenon in different ways. To address this question, we recorded the activity of single primary auditory cortical neurons (n = 423) in awake ferrets (n = 7) during the presentation of natural sound stimuli. We then fit STRFs incorporating one nonlinear contextual mechanism (GC or STP) or both mechanisms (STP+GC) on this single dataset. We compared model performance using the correlation coefficient (Pearson's R) between predicted and observed time-varying firing rate for each neuron. Our results indicate that there is no significant performance difference between the STP and GC models, but that the STP+GC model performs significantly better than either individual model. This finding indicates that the STP and GC models contain distinct explanatory power. Further, the success of the combined model hints that auditory cortical neurons utilize at least two independent mechanisms to adapt encoding properties to different sensory contexts. Future neuromorphic sound processing technologies may therefore improve their performance by incorporating both STP- and GC-based strategies.

45 Auditory Neurofeedback for Noise Suppression and Speech Enhancement

Yue Dong (1), Yan Gai (1)
(1) St. Louis University

Cortical entrainment refers to the synchronization of brain activity to external sensory stimuli. For speech input, electroencephalography (EEG) signals may be linearly related to the sound envelope (in the frequency range of 2 to 8 Hz) or other linguistic features. When speech is presented in background noise, our previous study found that brain signals obtained with certain electrodes can suppress response to noise and more or less maintain correlations to the speech component. Here we developed a neurofeedback system to explore if the human subject can actively enhance speech response and suppress noise response. A 64-channel EEG system was used to record brain signals while the subject was presented with speech sentences presented alone in noise. In contrast to conventional neurofeedback systems that mostly measure neural oscillations to monitor the brain's internal states, our system provided the subject with real-time correlations of ongoing EEG signals evoked by speech in noise to a target. This target was either the envelope of the speech alone or pre-recorded EEG evoked by speech alone. Subjects were asked to increase this correlation value by changing their attention or whatever technique they found effective. We observed diverse abilities of subjects in suppressing responses to the background noise. The EEG electrodes that provide the best correlations also differed. The next step of the study is to find out if the auditory neurofeedback training can increase speech intelligibility assessed with behavioral tasks.

46 The effect of lexical status on acoustic encoding in human auditory cortex: preliminary results form intracranial recordings

McCall E Sarrett (1), Kayleen Schreiber (1), Hiroto Kawasaki (2), Matthew A Howard III (2), Bob McMurray (3,4)
(1) Interdisciplinary Graduate Program in Neuroscience, University of Iowa
(2) Department of Neurosurgery, University of Iowa
(3) Department of Psychological and Brain Sciences, University of Iowa
(4) Department of Otolaryngology, University of Iowa

Speech perception is challenging. Fine-grained acoustic cues must be distinguished quickly to categorize the signal into phonemes. Psycholinguistics suggests listeners maintain fine-grained acoustic detail for longer than the fleeting moment it appears in the auditory signal (Connine, Blasko, & Hall, 1991; McMurray, Tanenhaus, & Aslin, 2008)—subsequent information can bias how listeners categorize ambiguous speech sounds. Further, listeners can use later top-down information about whether a stimulus makes a word to alter categorization (Ganong, 1980). For example, an ambiguous sound between /d/ and /t/ is perceived as a /d/ in the context of “dash” but a /t/ in the context of “task”. This requires listeners to maintain fine-grained detail throughout the word or later, and reinterpret this information using lexical status. Studies using fast optical imaging, EEG, and MEG suggest listeners maintain such detail for at least 200 msec (Toscano et al, 2018; Gwilliams et al, 2018; Sarrett et al, in prep). However, it is unclear exactly what brain regions are involved, and whether feedback from higher level areas alters extended auditory representations.

We used electrocorticography (ECoG) to address these questions using a variant of Ganong (1980). Participants heard minimal pairs manipulated along a continuum from /b/ to /p/ that differed by which endpoint formed a word. For example, “beach” and “peach” are equi-biased; “boke” and “poke” are p-biased (“boke” is not a word); and “bake” and “pake” are b-biased. Participants were four neurosurgical patients with medically intractable epilepsy who were undergoing chronic monitoring. Participants heard each token and categorized its initial sound. We used multivariate pattern analysis (support vector regression) to recover VOT from local field potentials (LFP) and high gamma activity (Nourski et al, 2015) in auditory and perisylvian language cortices. Preliminary analyses indicate that fine-grained acoustic cues can be recovered even from high level language processing hubs as late as 300 msec, and that there is an early time window when acoustic cues are processed independent of top-down factors. Analyses in later time windows suggest that lexical status feeds back even to the earliest levels of cortical processing.

47 **Efficient codes of the auditory nerves reconsidered with natural reverberations**

Hiroki Terashima (1), Shigeto Furukawa (1)
(1) NTT Communication Science Laboratories

Efficient coding has been a leading computational principle for the sensory neuroscience. Following the visual system, Lewicki (2002) argued that the auditory periphery can be explained by unsupervised learning of natural sounds. One of the study’s claims is that the basis optimized to code human voice resembles the auditory nerve fibres, whose filter sharpness distribution is preserved across mammals. We were able to reproduce the matched distribution by applying the same algorithm to clean recordings of human voices. However, we also found that an efficient code for human voices recorded in the natural environment shows much sharper tuning than the auditory nerve fibres, even though the environment recording is closer to the sensory signal our ears receive and more natural than a studio recording. Our analysis showed that the waveforms are distorted on a short time scale comparable to the time window of the auditory nerve filters and that the mismatch can be reproduced by simulating environmental reverberations. How can we better model the auditory periphery including the environmental modulations? Inspired by a recent work on the visual hierarchy (Yamins et al., 2014), we hypothesized that the auditory periphery is optimized to perform auditory tasks we face in the natural environment. To test this, we trained a five-layer deep convolutional neural network to classify phonemes based on their waveforms modulated by natural reverberations and white noise. After the training, the waveform filters learned in the first layer showed characteristics similar to the auditory nerve fibres, whereas a normal efficient code for the same input did not. The results suggest that the auditory periphery efficiently encodes task-related information rather than the incoming signal itself and that our understanding of sensory systems in the natural environment, not only the visual system, can be furthered by using a framework of task-based optimization.

48 Cooling of the auditory cortex modulates temporal processing of auditory thalamic neurons in awake marmosets

Yuanqing Zhang(1), Siyi Bai(1), Xiaohui Wang(1), Rui Li(1), Hao Sun(1) and Lixia Gao(1)
(1)Zhejiang University

Temporal information is essential for perception and discrimination of communication sounds, such as human speech and animal vocalizations. So far, it remains largely unknown the thalamocortical circuit mechanisms underlying sound temporal processing in awake animals. In the present study, single unit recordings were performed in medial geniculate body (MGB) when the primary auditory cortex (A1) of awake marmosets were reversibly inactivated by cooling technique. We found that cooling of A1 has great influences on the temporal processing of MGB neurons. Firstly. A1 modulated differently on the onset and sustained sound driven responses of MGB neurons: sustained and late phase auditory responses diminished when A1 was cooled and retrieved when the temperature recovered to normal whereas onset responses were less affected. The result suggests that onset responses of MGB neurons largely inherited from the ascending auditory inputs whereas their sustained responses were due to the cortical feedback. Our results also support the hypothesis that sustained responses of A1 neurons were generated by intracortical inputs instead of thalamocortical inputs. Regarding the temporal responses of MGB neurons to time-varying stimuli, we found that cortical cooling either enhanced the synchronized responses of MGB neurons to slow repetition rates or weakened the non-synchronized responses of other MGB neurons to fast repetition rates, which suggests that cortical feedback control changed the temporal coding schemes of MGB neurons to time-varying stimuli: cortical feedback weakened the ability of MGB neurons to use temporal coding instead strengthen their ability to use rate coding strategy.

49 Olfactory cue congruency modulates neuronal responses in primary auditory cortex

Omri Gilday (1,2), Adi Mizrahi (1,2)
(1) Hebrew Univ. of Jerusalem, Jerusalem, Israel
(2) Edmond and Lily Safra Center for Brain Sciences

The function of sensory cortex is classically perceived as representing bottom up sensory information from the environment. In recent years however, it is becoming increasingly accepted that cortical responses and perception in general are highly modulated in a non-bottom-up manner. Such modulations consist of contextual, attentional, motivational and expectation driven effects, among others. These might arise from local circuit computations, top-down modulation from cortical regions higher up the cortical hierarchy, neuro-modulatory sources etc. In addition, these modulations can be a result of the workings of hard-wired circuits or some experience dependent plasticity. Here we show an example of such non-representational modulation that results from cue congruency driven expectations.
We use olfactory stimuli as cues that precede auditory stimuli. We show neurons in auditory cortex that respond differentially to sound when the olfactory cue is congruent and when it is not. These findings show an example of what might be an expectation driven modulation of sensory cortical neurons. Moreover, this is an example of experience dependent learning of such modulation, and one that cannot be mediated by local circuitry since the origin of the cue is non-auditory. Next, we plan to identify both the characteristics of such experience dependent plasticity paradigm and the source of this modulation to auditory cortex.

50 Pupil response to rapid predictable auditory sequences

Alice Milne (1), Christina Tampakaki (1), Sijia Zhao (1), Maria Chait (1)
(1) University College London

The brain is highly sensitive to auditory regularities. We exploit the predictable order of sounds in many scenarios, from parsing complex auditory scenes to the acquisition of language. However, it remains difficult to study incidental auditory sequence learning. Pupillometry can be used across populations (e.g. infants and adults) and species (e.g. human and non-human primates); therefore, offering a potential technique to implicitly study sequence processing across different subject groups. However, it remains unclear exactly how sequence processing will be reflected in the pupil response.
Abrupt changes to the sequential structure of auditory sounds elicit a phasic pupil dilation response that is thought to reflect an arousal-based spike in norepinephrine. However, slower changes to pupil dilation (tonic response) are also observed. These tonic changes have been linked to the release of acetylcholine and hypothesized to be associated with learning processes.
Here we assessed if the predictability of a rapid stream of auditory tone pips modulates pupil diameter.
We presented either deterministic or random sequences of tones and systematically varied the number of different tone frequencies in each sequence. We additionally studied sequences with more variable predictability, and each experiment tracked pupil diameter while subjects completed an auditory task unrelated to the sequence structure.
Our findings demonstrate that predictability of an auditory sequence modulates changes in pupil diameter and thus shows the potential of this technique for implicitly studying auditory regularities across cognition. It paves the way for future work to probe the underlying neurochemical drivers and cognitive processes implicated in sequence processing.

51 Activity in auditory cortex predicts specificity of fear learning

Katherine C. Wood (1), Richard Betzel (1,2), Danielle Bassett (1), Maria N. Geffen (1)
(1) University of Pennsylvania
(2) University of Indiana

Auditory perception relies on learning-driven neuronal plasticity within the auditory pathway. Here, we investigated how associative learning, differential auditory fear conditioning (DAFC), affects neuronal population responses to sounds in auditory cortex (AC). In DAFC, the subject is presented with two different frequency tones, one of which is paired with a foot-shock. Previously, we found that AC is required for expression of DAFC-driven changes in sound-frequency discrimination acuity (Aizenberg and Geffen, 2013) and that modulating inhibitory neuronal activity in AC leads to similar bi-directional changes in discrimination acuity (Aizenberg, 2015). However, how DAFC affects tone-evoked population neuronal activity remained unknown. We hypothesized that DAFC would drive changes in population tone-evoked neuronal activity corresponding to either and increase or a decrease in neurometric frequency discrimination acuity, as a function of fear learning specificity.
To understand the transformation of sound representation in AC before and after DAFC we imaged calcium activity in hundreds of neurons simultaneously in AC of awake, head-fixed mice, tracking the same neurons over days under a two-photon microscope before and after two DAFC sessions.
We quantified changes in frequency-dependent responses of individual and populations of neurons. DAFC drove heterogeneous changes in individual neuronal responses for either paired or unpaired tone frequencies. However, on average, we found an increase in response at the conditioned frequency and a decrease at the unconditioned frequency. These changes resulted in an increase in Fisher Information at the unconditioned frequency, however, this was not correlated with learning specificity. We found that the proportion of cells responding to the conditioned tone after DAFC correlated negatively with the learning specificity. Using machine learning to calculate neural discrimination of the conditioned and unconditioned tones, we found that discriminability before fear conditioning predicted the learning specificity of each mouse. Neural discriminability after fear conditioning only showed a weak correlation with behavioral discriminability. These findings suggest that activity in auditory cortex is important for discriminating between frequencies during fear learning.

52 Variation in temporal coding of vocalizations along the anterior-posterior extent of marmoset auditory cortex

Xiao-Ping Liu(1), Xiaoqin Wang (1)
(1) Johns Hopkins University

To gain insight into functional properties of the multiple fields in primate auditory cortex, we examined the responses of neurons to vocalizations across the anterior-posterior extent along the lateral sulcus in the marmoset (Callithrix jacchus), a highly vocal monkey species. Studies that have ventured anterior to the primary auditory cortex (AI) have seen longer response latencies and temporal integration windows and a scarcity of neurons with well synchronized responses to click trains and sinusoidal amplitude modulation, suggesting that anterior field neurons transform periodic auditory patterns into a rate code (Bendor and Wang, 2008; Camalier et al., 2012; Scott et al., 2010; Wang, 2007). In this study, we examined time domain processing of natural stimuli in both anterior and posterior fields by recording single unit responses to a set of 20 marmoset call types as well as sets of exemplars of each call type. To quantify temporal precision of evoked spike trains, we calculated the correlation index (CI) of the responses to multiple presentations (Joris et al., 2006), which indicates the degree of temporal variability in spike timing between repetitions. A subset of low spontaneous rate neurons displayed high CI values indicating timing variability less than a millisecond in response to some vocalizations. These neurons tended to have onset responses and be more prevalent in the posterior region. While the anterior region generally lacked such temporal precision, it featured other specializations, such as an area enriched in neurons with narrow frequency tuning, selectivity for slowly modulated vocalizations like phee calls, and robustness to broadband background noise. These specializations may form parallel forms of processing, for example, integrating across spectrum to enhance temporal resolution for detection of temporal edges or integrating across time to enhance selectivity for slower features. Neurons with higher and lower CI values responded in diverse ways to different exemplars of the same call types and may respectively use temporal or rate codes to encode these calls. These observations are reminiscent of recent studies in humans showing anterior-posterior differences in temporal responses along Heschl's gyrus or superior temporal gyrus (Hamilton et al., 2018; Hullett et al., 2016; Jasmin et al., 2019; Norman-Haignere et al., 2015; Santoro et al., 2014), suggesting this may be a conserved organization of the primate auditory cortex. These parallel processing strategies may help identify temporal and spectral features that are key to speech or music processing as well as animal communication sounds.

53 Relationship between saccade-related eardrum oscillations and clinical measures of middle ear impedance

Cynthia King(1), Rachel Landrum(1), David Murphy(1), Stephanie Schlebusch(1), David Kaylie(2), Christopher A. Shera(3) and Jennifer Groh(1,4,5)
(1)Duke University Center for Cognitive Neuroscience
(2)Duke University Department of Surgery, Division of Head and Neck Surgery and Communication Sciences
(3)University of Southern California
(4)Duke University Department of Psychology and Neuroscience
(5)Duke University Department of Neurobiology

Integration of auditory and visual information is necessary in order to make sense of the world around us. How and where this integration occurs within the brain is not known. Our laboratory has identified a phenomenon where, in the absence of auditory stimuli, both eardrums begin synchronous, low-frequency oscillations just prior to saccadic eye movements. These eye movement-related eardrum oscillations (EMREO) change in amplitude and phase with changes in saccade magnitude and direction. This discovery suggests that connections between the visual and auditory systems likely begin as early as the auditory periphery (Gruters, Murphy et al, PNAS 2018). Ongoing work in non-human primates can provide insights into potential anatomical mechanisms (Schlebusch et al, Advances and Perspectives in Auditory Neuroscience conference 2018; Schlebusch et al, Society for Neuroscience conference, 2019) and examining the response in different human clinical populations can also further our understanding of the underlying mechanisms and potential utility of these oscillations.

To further characterize this phenomenon in humans and assess the feasibility for use in future clinical research, we examine the relationship between traditional measures of middle-ear function (e.g., compliance) and characteristic features of the EMREO. Normal hearing subjects participated in visual tracking tasks, divided into one-hour sessions across several days. Subjects were seated, facing a monitor, and stable head position was maintained using a chinrest. Microphones placed in both ear canals recorded the oscillations. Eye movements were tracked with a video eye tracker. Analysis shows a reliably recorded EMREO in approximately 5 minutes of recording time, suggesting potential value in future clinical research. Middle-ear tympanometric measurements were obtained prior to each recording session, allowing the investigation of the relationship between variations in middle-ear measurements and the structure of the EMREO. The impact of altered visual or auditory input on the response is examined."

54 Short-term effects of vagus nerve stimulation on auditory learning and stimulus-specific activity in auditory cortex

Jesyin Lai (1), Stephen V David (1)
(1) Oregon Health and Science University

Previous studies of vagus nerve stimulation (VNS) have shown that chronic stimulation can facilitate central plasticity, e.g. enhancing the rate of motor rehabilitation following stroke or producing stimulus-specific changes in auditory cortical selectivity. VNS is believed to trigger release of neuromodulators, including norepinepephrine and acetylcholine, which may mediate the associated plasticity. Most previous work has studied the effects of chronic VNS over many days. To study short-term VNS effects, we measured its effects on learning and auditory cortical activity following brief, acute periods of stimulation. We implanted cuff electrodes onto the vagus nerve of ferrets and trained them by classical conditioning to associate one specific target sound (T1) with a reward and another target sound (T2) with no reward. T1 and T2 were changed every 2 days (200-250 trials/day), typically after reward associations were learned. When T1 and T2 were paired with VNS (1 s duration, 30 Hz, 200 us biphasic pulses, 0.4-2 mA, VNS onset 100-150 ms before T1/T2 onset), rates of learning the reward association increased on day 1, regardless of task difficulty. In contrast, animals' learning rates were lower when VNS occurred randomly during the silence after T1/T2 presentation (non-paired condition). Afferent VNS pathways involve nuclei that mediate arousal, which is reflected by changes in pupil size. A phasic pupil dilation was observed for several seconds following VNS, suggesting an increase in arousal that may support the greater learning efficiency. To measure effects of VNS on cortical activity, we recorded neurophysiological single- and multi-unit activity in primary auditory cortex of passively listening animals pre- and post-VNS. Neural responses in a subpopulation of neurons were decreased in the condition after pairing VNS with the best frequency tone. Neural activity was also positively correlated with pupil size. Regressing out effects of pupil-indexed arousal decreased the response difference of post- versus pre-VNS. However, significant reduction of neural responses remained in post-VNS. This outcome contrasted with previous findings, which have generally reported enhancement of stimulus-specific responses after long-term VNS. This difference may reflect the short timescale of VNS (20 times per tone, i.e. about 10 min) in our study. Taken together, the results of this study support a role for VNS in auditory learning and help establish VNS as a tool to facilitate neural plasticity.

55 Extensive psychophysical and neural comparisons of deep neural networks to human hearing

Alexander J.E. Kell (1,2,3), Erica N. Shook (1,2,3), Josh H. McDermott (1,2,3,4)
1. Department of Brain & Cognitive Sciences, MIT
2. McGovern Institute for Brain Research, MIT
3. Center for Brains, Minds, & Machines, MIT
4. Program in Speech and Hearing Biosciences and Technology, Harvard University

Despite their recent renaissance, the extent to which deep neural networks are viable models of biological sensory systems remains unclear. To probe potential similarities and differences with the human auditory system, we simulated a large set of psychophysical and fMRI experiments on a deep network trained to recognize speech and music. Psychophysically, the network generalized like humans for several classes of unnatural speech manipulations, e.g., locally reversed speech (Saberi & Perrott, 1999) and inharmonic speech (Popham et al., 2018). However, the network failed to generalize at human levels for other stimulus alterations: whispered speech, speech in reverberation, and time-compressed and -dilated speech, most of which occur in everyday environments and thus are likely familiar to humans (but which were not in the network's training set). Introducing a simple approach to simulating fMRI experiments with deep networks, we found that averaged network layer activations reproduced the results of several human neuroimaging studies. The similarities between network and human suggest that deep neural networks can replicate aspects of human audition, and the discrepancies revealed here suggest targets for future modeling efforts.

56 Targeted cortical manipulation of auditory perception in a challenging sound discrimination

Sebastian Ceballo (1), Zuzanna Piwkowska (1) (2), Jacques Bourg (1), Aurélie Daret (1) and Brice Bathellier (1)
(1) Paris-Saclay Institute of Neuroscience (NeuroPSI), Department for Integrative and Computational Neuroscience (ICN), Université Paris-Saclay and Centre National de la Recherche Scientifique, Gif-sur-Yvette, F-91198, France
(2) Present address: Institut Pasteur, Dynamic Neuronal Imaging Unit, Paris, France.

Driving perception by direct activation of neural ensembles in cortex is a necessary step for achieving a causal understanding of the perceptual code and developing central sensory rehabilitation methods. Here, using optogenetics manipulations during an auditory discrimination task in mice, we show that auditory cortex can be bypassed by coarser, eventually faster pathways for simple sound identification. Yet, when the sensory decision becomes more complex, involving temporal integration of information, auditory cortex activity is required for sound discrimination and targeted activation of specific cortical ensembles change perceptual decisions as expected from our read out of the cortical code. Hence, auditory cortex representations contribute to sound discriminations by refining decisions from parallel routes.

57 Fundamental response properties of auditory cortical activity in Heschl's gyrus of children as observed from direct intracranial recordings

Mitchell Steinschneider (1), Ariane E. Rhone (2) , Kirill V. Nourski (2), Christopher K. Kovach (2), Brian J. Dlouhy (1)
(1) Albert Einstein College of Medicine
(2) *University of Iowa*

Improvement in technology and techniques has led to a greater use of neurosurgical interventions for remediation of medically intractable epilepsy in children. To clarify developmental features of audition, investigations into fundamental functional properties of auditory cortex in children have been initiated. These studies follow on the heels of previous investigations in adult patient-subjects (reviewed in Nourski, Laryngoscope Investig Otolaryngol 2017, 2:147-56), permitting comparisons between auditory cortical physiology in children and adults.

Seven children were studied (3-18 years of age). All studies were approved by the NIH and University of Iowa Institutional Review Board. Informed consent was provided by the children's parents or legal guardians. Verbal assent was obtained from children ages 5-9, and written assent was obtained for older children. The 3-year-old child was studied only with passive presentation of stimuli and in the presence of a parent who could terminate research activities at any time. The 18-year-old provided his own informed consent. Depth electrodes targeting posterior insular cortex for seizure monitoring were placed in all subjects, permitting recordings from Heschl's gyrus or its immediate vicinity (4 left hemisphere, 5 right hemisphere). Click trains (repetition rates 25-200 Hz), pure tones (frequencies 0.25-8 kHz, and stop consonant-vowel syllables were presented. Analyses focused on local field potentials and event-related high gamma power.

In common with adult subjects, response latencies progressively increased and high gamma power progressively decreased from posteromedial towards anterolateral Heschl's gyrus. Individual cortical sites were generally broadly tuned but did exhibit spectral preferences within the frequency range of the tones. Similar to adults, frequency-following responses (FFR) elicited by click trains were generally observed for rates up to 50–100 Hz and were maximal at the most posteromedial sites. FFR to the fundamental frequency of the speech syllables (~100 Hz) was especially prominent in posteromedial Heschl's gyrus.

We conclude that many fundamental properties of neural activity recorded from Heschl's gyrus are similar to those seen in adult subjects from early childhood onward."

58 Transformations of sound representations from the cochlea to the auditory cortex

Jacques Bourg (1), Alexandre Kempf (2), Thibault Tarpin (3), Jerôme Bourien (4), Jean-Luc Puel (5), Brice Bathellier (6)
(1) Department for Integrative and Computational Neuroscience (ICN) UMR9197 CNRS / University Paris Sud
(2) Department for Integrative and Computational Neuroscience (ICN) UMR9197 CNRS / University Paris Sud
(3) Ecole Normale Supérieure, PSL.
(4) University of Montpellier
(5) University of Montpellier
(6) Department for Integrative and Computational Neuroscience (ICN) UMR9197 CNRS / University Paris Sud

The auditory system is thought to be hierarchically organized encoding increasingly complex features from peripheral to more central stages. Yet the precise transformations of auditory representations across stages of the most central auditory system are not fully characterized. To start addressing this question in a systematic manner, we used two-photon calcium imaging in awake mice to extensively record auditory responses in the auditory cortex (AC, at depths ranging from 0-600 µm) and the superficial layers of the inferior colliculus (IC, 0-200 µm). To capture both spectral and temporal aspects in auditory coding, we used a wide range of laboratory sounds including pure tones, chords, intensity ramps, amplitude modulated sounds and various frequency chirps. We thereby collected a dataset of 59590 neurons (7 mice, 60 sessions) in the AC, fully sampling the horizontal extent of AC, as assessed with global tonotopic mapping. We also obtained activity from 15311 neurons in the IC (31 mice,101 sessions). In addition, we simulated the responses to these sounds using a detailed auditory nerve model (Meddis 2005).

We asked how the population patterns of couples of closely related sounds differed in the cochlea, the IC, and the AC: population patterns evoked by pure tones at 60 dB vs 80 dB, by up vs down-ramping pure tones, by up vs down frequency chirps and by sums of ramps vs the summed activity of the ramps presented in isolation. We show that the population patterns elicited by all these different sounds are progressively decorrelated along the sensory hierarchy, and explicit the origins of the divergent representations. For instance, representations of pure tones at different intensities diverge strongly between IC and AC: in IC neurons either rapidly reach a response plateau or monotonically increase their response with intensity. In AC it is possible to identify three large neuronal populations non-monotonically tuned to different levels of intensities (typically 60,70, 80dB). We also show a very strong sub-linearity of the reponses in the cortex to chords of several harmonics, with respect to the sum of the activity when these are presented in isolation.

Together these results point towards the progressive emergence of a coding scheme in auditory cortex which captures different temporal features of the sounds into distinct neuronal activity patterns, possibly contributing to perceptual segregation of these features.

59 Sound Representation in the Mouse Temporal Association cortex (TeA)

Libi Feigin(1), Gen-ichi Tasaka(1), Ido Maor(1) and Adi Mizrahi(1)
(1) Edmond and Lily Safra Center for Brain Sciences, Hebrew University of Jerusalem

Background
Temporal association cortex (TeA) is ventral to the secondary auditory cortex and dorsal to the Rhinal fissure. Only few studies reported the activity from TeA in response to sounds. TeA was reported to be tonotopically organized and suggested to be invariant to frequency and temporal modulations of natural sounds. But otherwise, TeA remains largely unstudied.
Results
To define the inputs to TeA, we first performed monosynaptic retrograde rabies tracing from starter cells in TeA. We found a surprisingly large number (>100) of brain regions projecting into TeA including cortical and subcortical regions. Quantitative analysis of the connectivity into TeA showed that the primary auditory cortex (A1) is its most prominent source of input (~45% of TeA's total inputs). We, thus, recorded spiking activity from TeA with reference to A1.
To define the physiological responses of TeA to sounds, we used the newly developed high density multielectrode array "Neuropixels". We recorded spiking activity from A1 and TeA simultaneously in ketamine anesthetized as well as in head restrained awake mice. An initial analysis shows that representations of pure tones are surprisingly similar in A1 and TeA. TeA spans a similar frequency range and response bandwidth to that of neurons in A1. Interestingly, neurons in TeA exhibit higher response latencies. For example, units in layer 5/6 have mean latencies that follow A1 by ~50 msec. Signal correlations, calculated for pure tone stimuli as well as complex sounds, and noise correlations are slightly elevated within units in TeA compared to units in A1. We are currently analyzing population responses within and across regions to uncover the transformation of sound representation from A1 to TeA, under normal condition and following experience dependent plasticity.
Conclusions
Our work shows that TeA is a higher order auditory field directly downstream of A1. The diverse connectivity into TeA, and its physiological signature suggests that this brain region sub-serves higher order auditory computations.

60 Functional Connectivity Between Cortical and Subcortical Auditory Regions: Examining voxel-wise connectivity during rest and the movie paradigm

Chad R. Buckland, Mark O'Reilly, Dr. Ingrid Johnsrude
University of Western Ontario

Functional connectivity (FC) analyses have been used to examine the functional organization of spatially distinct brain regions in a variety of functional magnetic resonance studies, including task-based and task-free rest. Movie watching during scanning has provided a tool for overcoming the limitations presented by the unconstrained nature of resting-state studies, including pragmatic concerns over movement. However, the movie paradigm may also present advantages when examining connectivity in sensory regions, particularly in the auditory network. We examined connectivity between five auditory seed regions in the cortex, (primary auditory cortex, medial belt, lateral belt, parabelt and area 55b) and 4 subcortical seed regions (inferior colliculus, medial geniculate body, caudate and nucleus accumbens) in healthy adults (n=80), using the Human Connectome Project (HCP) dataset (15 min resting state; 15 min rest). Connectivity values were significantly higher during movie watching than at rest in cortical auditory seed regions, particularly in area 55b, an area implicated in language tasks. Additionally, given their role in auditory processing, FC to the inferior colliculus and medial geniculate body was examined, showing similar connectivity values. Movie watching appears to generate more robust connectivity values in auditory regions than does the resting state. These connectivity differences may be driven by differences in the amplitude of BOLD signals, and interindividual variability in connectivity, between conditions. Movie-driven fMRI is suggested as a tool for future studies of auditory network organization.

61 Infant neural response to speech and tones

Bonnie K. Lau (1), Samu Taulu (1), Patricia K. Kuhl (1), Adrian KC Lee (1)
(1) University of Washington

The human central auditory system is characterized by a protracted and extended period of development. While infants begin responding to sound in the third trimester of gestation, significant cortical immaturity is observed throughout infancy. Infants' ability to discriminate sounds in both speech and music from birth is well documented; however, the neural mechanisms that support early auditory perception are not well understood. Here we use magnetoencephalography (MEG) with recent advancements in movement compensation to obtain functional measures of sound processing in awake infants. We recorded MEG responses to a bi-syllabic English word ("baby"; speech condition) and a complex pitch change (160 to 200 Hz; tone condition) in infants at 3 months and again at 6 months of age. Each trial consisted of a 2-s stimulus with a pitch or syllable change at 1 s. The change midway was introduced to enable tracking of the neural response through both signal onset and the acoustic change. We also administered clinical assessments of gross motor, visual reception, fine motor, language, and adaptive function. The information gathered from these standardized assessments will allow us to characterize cross-domain functional changes in development that occur with changes in the neural processing of sound. Preliminary data analysis shows that robust, temporally precise MEG signals with high signal-to-noise ratios can be recorded in response to speech and tones at both 3 and 6 months of age. Furthermore, the longitudinal approach will allow us to observe change over time in the same infant and provide an estimate of both within and between subject variability.

62 Binaural hearing in the naked mole-rat

*E. MCCULLAGH1, J. PEACOCK1, A. KLUG1, T. PARK2, D. J. TOLLIN1;
1Dept. of Physiol. and Biophysics, Univ. of Colorado Anschutz, Aurora, CO; 2Biol., Univ. of Illinois Chicago, Chicago, IL

The Naked mole-rat (Heterocephalus glaber) is increasingly being used as a laboratory mammal due to its resistance to aging and cancer, as well as other peculiar traits. The mole-rats live in eusocial, underground colonies of around 80 animals. The underground tunnels in which they live limit the range of acoustical information the animals are exposed to. Sounds propagate well through the burrow, but there are very limited sound localization cues. However, the mole-rats do produce a wide range of vocalizations for communication, suggesting that sound, and thus hearing, plays an important role in their lives.

Previous studies have suggested that mole-rats have a degenerate hearing system. Published behavioral measurements show poor hearing thresholds, limited high frequency hearing, and poor sound localization abilities. And published anatomical measurements have shown intraspecific variations in middle and inner ear structures. Further studies have also shown that the mole-rats lack the HCN1 ion channel from binaural nuclei, which contributes to the integration of binaural inputs in the brainstem, thus potentially impeding their ability to effectively localize sounds.

In order to provide a more comprehensive understanding of hearing and sound localization ability in mole-rats, we made various anatomical and physiological measurements. Specifically, we made measurements of the binaural interaction component (BIC) of the auditory brainstem response (ABR), which is a non-invasive electroencephalographic signature of neural processing of binaural sounds by brainstem neurons. We report that naked mole rats do have a measurable BIC of the ABR similar to other laboratory species commonly used for sound localization research. However, it is markedly variable across individuals. On the other hand, the BIC varied with interaural time difference, suggesting an ability to localize sound. Additionally, we performed histological analysis to investigate the underlying neuroanatomy of the brainstem of these peculiar mammals. In conclusion, the naked mole rat may have a more refined auditory brainstem than previously shown, making them an interesting species for future sound localization research."

63 Multiple Temporal Integration Windows for Sound Statistics

Richard McWalter (1), Josh H. McDermott (1)
(1) Massachusetts Institute of Technology

Sound textures, as arise from falling rain or galloping horses, are thought to be represented in the auditory system with time-averaged statistics measured from early auditory representations. Recent work has suggested that texture statistics can be averaged over integration windows as long as several seconds [McWalter and McDermott, 2018]. However, it remains unclear whether all statistics are averaged over the same extent, or whether averaging windows might vary across statistics, potentially adapted to the variability of the statistic. We measured integration windows for individual classes of statistics from a standard auditory texture model [McDermott and Simoncelli, 2011]. In a psychophysical experiment, listeners judged which of two sound textures was most similar to a reference texture. We measured performance for different stimulus durations, using textures synthesized to vary in individual classes of statistics. In all cases, texture discrimination improved with stimulus duration but then leveled off, presumably signaling the extent of the averaging window used to estimate the statistics. However, the performance asymptote occurred at different durations for different statistics, ranging from ~150 milliseconds for the cochlear envelope mean (capturing the spectrum) to a few seconds for the power of low-rate modulation filters. The results suggest that the extent of time averaging varies depending on the statistic, as might be required to obtain stable estimates of functions differing in intrinsic variability.

64 Characteristics of Human Pitch Perception Emerge in Neural Networks Optimized to Estimate F0 from Natural Sounds

Mark R Saddler (1), Ray Gonzalez (1), Josh H McDermott (1)
(1) Massachusetts Institute of Technology

Despite a wealth of psychophysical data, developing computational models that account for pitch perception has proven challenging. In human listeners, the pitch of a sound depends on both spectral and temporal information available in the auditory periphery, but the relative contribution of the various cues and the reasons for their varying importance remain poorly understood. We investigated whether the properties of human pitch perception would emerge simply from optimizing a general-purpose architecture to estimate fundamental frequency (F0) from cochlear representations of natural sounds. We trained a convolutional neural network to classify simulated auditory nerve representations of speech and instrument sounds according to their F0. An established model of the auditory periphery (Bruce et al. 2018) was used to simulate the instantaneous firing rate responses of 50 auditory nerve fibers. Once trained, we simulated psychophysical experiments on the network. Pitch discrimination thresholds measured from the trained neural network replicated many of the known dependencies of human pitch discrimination on stimulus parameters such as harmonic composition and relative phase. Discrimination thresholds were best for stimuli containing low-numbered harmonics that were resolved by the cochlear filters and increased for stimuli containing only higher-numbered, unresolved harmonics. Randomizing the relative phase of harmonic components worsened pitch discrimination performance only when harmonics were unresolved, indicating the network learned to use temporal cues for pitch extraction when spectral cues were unavailable. Furthermore, the trained network qualitatively replicated human pitch judgments on a number of classic psychoacoustic manipulations (pitch-shifted inharmonic complexes, mistuned harmonics, transposed tones, alternating-phase harmonic complexes). We also simulated neurophysiological experiments on the trained network and found units in the later convolutional layers that exhibited pitch-tuning and selectivity for either resolved or unresolved harmonics. To better understand how the dependencies of pitch perception arise from either constraints of the peripheral auditory system or from statistics of sounds in the world, we independently manipulated parameters of the peripheral model and the training corpus, and found that each altered the network's performance characteristics. The results collectively suggest that human pitch perception can be understood as having been optimized to estimate the fundamental frequency of natural sounds heard through a human cochlea.

65 Pitch provides a compact code for memory storage

Malinda J. McPherson (1), Josh H. McDermott (2)
(1,2) Department of Brain and Cognitive Sciences, MIT
(1,2) Program in Speech and Hearing Biosciences and Technology, Harvard University
(2) McGovern Institute for Brain Research, MIT

Perceptual systems have limited capacity and must summarize stimuli into compressed representations. Here we report that pitch, the perceptual correlate of a sound's fundamental frequency (f0), serves as a compact code for auditory memory. We compared discrimination of harmonic sounds (whose spectra can be summarized with a single f0) to discrimination of inharmonic sounds (whose spectra are not thus compressible). When sounds were back-to-back in time, discrimination thresholds for the two stimulus types were similar. But when sounds were separated by time delays, discrimination was better for harmonic sounds, indicating a dependence on f0-based pitch for storing information over time. To probe the underlying mechanisms, we examined individual differences in pitch discrimination thresholds for harmonic and inharmonic tones across large sets of participants tested online, both with and without silent pauses between the tones being compared. Pitch discrimination thresholds for harmonic and inharmonic tones were strongly correlated when the notes were not separated by a pause, but this correlation decreased when a three second silence was added between tones. The results suggest that listeners detect pitch changes between contiguous tones by directly comparing the spectra of the sounds, but transition to comparing f0s when sounds must be stored over a delay. The results are suggestive of two different mechanisms for perceiving pitch information: one which does not estimate f0 and is important for local comparisons, and a second which summarizes harmonic frequency spectra with their f0 and is essential for memory storage.

66 Functional Architecture of Auditory Cortex in Awake Marmosets revealed by Multi-scale Multi-modal optical Imaging

Xindong Song (1), Yueqi Guo (1), Chenggang Chen (1), Xiaoqin Wang (1)
(1) Johns Hopkins University

The common marmoset (Callithrix jacchus), a highly vocal New World monkey species with a largely flat brain surface, has emerged in recent years as a promising non-human primate model for neuroscience research. Unlike most of the Old World primates, a significant proportion of auditory cortex in marmosets is directly accessible under the skull with optical imaging methods. Here, we applied wide-field enhanced intrinsic imaging, wide-field calcium imaging, and nearly silent two-photon calcium imaging methods in awake marmosets to study the functional architecture of auditory cortex. Previous studies have shown that primate auditory cortex consists of three layers of hierarchy, the core, the belt, and the parabelt. Responses to pure tone stimuli were largely confined to the putative core region through wide-field imaging. The low-frequency tonotopic reversal between A1 and R was clearly seen in all subjects. By increasing the bandwidth of sound stimuli, the responsive areas grew more laterally towards putative belt region, suggesting the belt region preferentially responds to a wider spectral content and may carry out spectral integration over a broad frequency range. Variety of natural sounds can elicit responses that collectively cover the entire superior temporal gyrus (STG). However, data from wide-field calcium imaging revealed that the area close to superior temporal sulcus (STS), putatively the parabelt, carried more spontaneous or endogenic rhythm that appeared largely independent of sound stimulation. This form of rhythm may reflect the behavioral state of the subject. Zooming into the fine details, the general response patterns within each two-photon field-of-view were consistent with wide-field imaging results. However, individual neurons' responses can be heterogeneous even for nearby neurons. The multi-scale multi-modal optical imaging approach reported here thus provides a new experimental paradigm for mapping the functional architecture of auditory cortex in awake condition in a high throughput way over conventionally electrophysiology methods.

Research support: NIH DC003180

67 The caudal paralaminar thalamus plays a critical role in cortical activation and arousal

Yiwei Wang(1), Ling You(1), Jingshan Zou(2), Rouyu Chen(1), Meijie Li(1), Miaomiao Liu(1), Dongqin Cai(1), Fenghua Xie(1), Yin Yue(1), Tianyu Li(1), Kexin Yuan(1)

(1)Department of Biomedical Engineering, School of Medicine, IDG/McGovern Institute for Brain Research, Center for Brain-Inspired Computing Research, Tsinghua University, Beijing, 100084, China.

(2)Department of Otolaryngology, WeiFang Medical University

Traditionally, the thalamus, the paramedian region in particular, is considered as an important node of the dorsal pathway of the ascending reticular activating system (ARAS), which plays a crucial role in maintaining behavioral arousal and wakefulness. Whether other thalamic nuclei are also critically involved in arousal and wakefulness remains largely elusive. Both our and other groups' tracing studies in mice showed that the posterior intralaminar thalamus (PIN) and peripeduncular nucleus (PP), which belong to the caudal paralaminar thalamus, receive direct and prominent inputs from brainstem reticular formation as well, suggesting their participation in arousal control. Using fiber photometry and EEG/EMG recordings, we found that the activities of PIN/PP VGluT2-positive neurons were high during wakefulness and REM sleep and low in NREM sleep, and increased before cortical activation at the sleep-to-wake transition. Optogenetic activation of PIN/PP neurons with low light power rapidly and reliably awoke animal's sleep and consistently produced cortical activation during general anesthesia, whereas optogenetic inhibition of PIN/PP neurons dramatically reduced the probability of awakening by acoustic stimulation. Moreover, we demonstrated that the projections from PIN/PP to temporal association cortices were critical for arousal regulation, very different from the working mechanism of the midline thalamus. Our findings indicate that the caudal paralaminar thalamus should also be considered as an important component of the dorsal pathway of the ARAS.

68 RESULTS OF SURGICAL TREATMENT OF NEUROMAS OF THE AUDIOUS NERVE WITH STEM GROWTH AND THE USE OF A COMBINED METHOD.

V.A. Pyatikop1 V.I. Sipityy 3, V.A. Chmut1, P.V. Lakhtin3, V.N. Kutsyn3, A.V. Genkin2, Kytovoi I.A.

1 Department of Neurosurgery, Kharkiv National Medical University, Kharkiv, Ukraine
2 Neurosurgical Department, Kharkiv Regional Clinical Hospital - Center for Emergency Medical Aid and Disaster Medicine, Kharkov, Ukraine
3 Kharkiv Medical Academy of Postgraduate Education, Kharkov, Ukraine

Purpose. Analyze the results of surgical treatment of patients with stem neuromas of the auditory nerve using intraoperative video endoscopy, microsurgery, ultrasound scalpel and intraoperative monitoring of the functional activity of the brain stem using the DX-NT-32 computer complex.
Materials and methods. The work is based on the analysis of the examination of 71 patients. Used for diagnostics: magnetic resonance imaging (MRI) with angiography (MRA) spiral computed tomography (CT) computer system DX-HT-32 for monitoring the functional activity of the brain stem.

The histological structure of the tumor corresponded to the neuroma of the auditory nerve. Of the 71 women surveyed, there were 42 and men 29 people.
In size, tumors were divided into 4 types: small to 10 mm in 10 PATIENTS, medium to 10 to 30 mm in 25 PATIENTS, BIG from 30 to 50 mm. in 30 patients gigantic, from 50 mm. in 6 patients.
The topographic and anatomical parameters of the ear, size, density, degree of germination and vascularization were determined using SCT, MRI, MR data. Accordingly to the obtained data was chosen for operational access I — suboccipital: 62 patients (87.3% ± 4: 35%), II - unilateral transientorial suboccipital craniotomy: 9 patients, (12.7% ± 0.6%).
The tumor was removed intracapsularly using video endoscopy and microsurgery and with a fragmentary method by ultrasonic scalpel totally or subtotal. During the operation, the registration of bioelectrical activity of the stem brain regions was carried out, using a DXNT-32 computer system, which allows to correct the course of the operation and prevent complications.
Results. The total removal of neuromas was made in a patient 35 (49.3% ± 2.5%), subtotal in a patient 32 (45.7% ± 2.4%), partial in patients 4 (5.6% ± 0.3%) The anatomical integrity of the facial nerve was preserved in 65 (91.5% ± 4.3%) patients. After the operation, good results were observed in cases of 50 (70.42% ± 3.52%), in 17 satisfactory (23.9% ± 1.09%), unsatisfactory with a lethal outcome in 4 (5.6% ± 0 3, 28%) cases. Functional outcomes were assessed on the Karnofsky scale — from 71 patients in terms of up to 10:50 years (70.42% ± 3.52%), they returned to their previous occupation, 17 (23.9% ± 1.09%) had activity partially restricted.
Group 4 (5,63 PATIENTS ± 0,28%) was selected in which the development of ischemic disorders in the brainstem with edema and dislocation after surgical treatment took place. The identified risk factors for the development of complications in the removal of patients' tumors can be taken into consideration when choosing surgical tactics and help develop ways to prevent them.
Findings.

1. The use of intraoperative video endoscopy in combination with microsurgery and an ultrasonic scalpel to remove the parastolic neurine of the auditory nerve is a highly effective radical method that reduces the percentage of mortality and help to achieve short postoperative rehabilitation period.
2. Neurophysiological intraoperative monitoring using the DXNT-32 computer system allows for the correction of the course of operations to prevent intraoperative complications.

Key words: stem neurinomas, CT, MRI, MRA microsurgical method, CTEEG monitoring, video endoscopy.

69 Mapping experience-dependent changes in sensorimotor representations across mouse auditory cortex

Samuel A M Picard (1), Yves Weissenberger (1), Andew J King (1), Johannes C Dahmen (1)
(1) University of Oxford

Ongoing activity in sensory cortex is not only determined by incoming sensory signals, but it is also influenced by a variety of contextual variables, such as an animal's movements and behavioural state. Many of these variables have been assumed to reflect a general cortical state shift that is relatively unaffected by experience, such as locomotion-induced gain changes in visual and auditory cortex. However, recent work has suggested that a subset of movement-related signals in auditory cortex may reflect the learned anticipation of the specific acoustic consequences of the animal's actions, such as its vocal output or the sounds of its footsteps. How these cortical sensorimotor representations are topographically organised, and how they change as a function of experience is currently unclear.
Here, a closed-loop auditory locomotion paradigm for head-fixed mice was developed, in which running speed was directly mapped onto sounds ordered along a perceptually uniform frequency axis. We performed chronic two-photon imaging experiments on Camk2a-Cre;Ai95d mice expressing the calcium indicator GCaMP6f in excitatory neurons, allowing us to track hundreds of neurons in layer 2/3 over weeks of exposure to a novel auditory environment. This revealed a variety of contextual modulations of auditory responses across different cortical subfields. Some of these modulatory effects were found to change over time as a function of experience. Results point towards a role for secondary auditory cortex in linking movements to sound, even when the relation between motor action and auditory feedback is arbitrary and newly learned.

70 Encoding vocalizations in background sounds at the cocktail party and in the woods

Delaina Pedrick (1)(2), Xiu Zhai (1)(3), Fengrong He (1)(2), Ian Stevenson (1)(4), Monty Escabi (1)(2)(3)
(1) University of Connecticut
(2) Department of Biomedical Engineering
(3) Department of Electrical Engineering
(4) Department of Psychological Sciences

Separating foreground sounds from background noise has long been the focus of the cocktail party conundrum. The goal of this study is to determine how the spectrum and modulation content of a background sound mask the neural encoding of a foreground vocalization. To evaluate the ability of certain sounds to mask vocalizations, natural and man-made background sounds were used as maskers (speech babble, construction noise, multi bird calls, babbling water, etc). Neural responses were recorded from the un-anaesthetized, head fixed Dutch Belt rabbit, in response to foreground vocalizations (speech and bird song) in the presences of the original and perturbed background sounds. To isolate the masking effects due to spectrum content, background sounds were phase randomized, which preserves the original sound spectrum but removes the modulation content. Alternatively, the modulation masking effect was isolated by spectrum matching all the background sounds to pink noise (1/f spectrum). This manipulation preserves much of the modulation content. Single neuron spiking data from the Inferior Colliculus in response to vocalizations paired with original, spectrum matched and phase randomized background sounds was analyzed to determine how the encoding of the foreground sound was affected by different background conditions. Shuffled correlogram procedures were used to isolate the background driven and vocalization driven components of the neural activity. Background driven activity was obtained by shuffling correlograms across frozen background sound segments with unfrozen foreground vocalizations (same background sound excerpt, different foreground excerpts). Alternately, foreground driven activity was obtained by shuffling correlograms across frozen foreground sound segments with unfrozen backgrounds (same foreground sound excerpts, different background excerpts from the same recording). Preliminary results show that spectrum of the background sound has a strong modulatory effect on the response firing rates. On the other hand, the modulation content of the background sound affects the reliability and precision of firing of both the foreground and background response. Thus, the sound modulation spectrum can influence the detailed temporal firing pattern to foreground sounds beyond what is expected for pure spectral masking. The findings suggest that high-order modulation content of sounds is affecting the neural representation of vocalizations in a variety of natural and man-made background sounds and thus is a critical acoustic cue for detecting signals in the presence of noise.

71 **Oscillatory Correlates of Auditory Working Memory using Electrocorticography** Joel Berger (1), Phillip E. Gander (1), Sukhbinder Kumar (2), Kirill V. Nourski (1), Matthew I Banks (3), Hiroyuki Oya (1), Hiroto Kawasaki (1), Matthew A. Howard III (1), Timothy D. Griffiths (1,2,4)
(1) The University of Iowa
(2) Newcastle University
(3) University of Wisconsin, Madison
(4) University College London

Working memory is the capacity to hold and manipulate behaviorally relevant information in mind in the absence of ongoing sensory input. Here we explored the hypothesis that working memory for tones requires a network of oscillatory activity in auditory cortex, frontal cortex, and hippocampus, and examined the form of such activity in neuronal ensembles.

We recorded local field potentials from six human subjects undergoing invasive monitoring for presurgical localization of epileptic foci. The subjects were implanted with depth electrodes along the axis of Heschl's gyrus (HG) containing primary cortex in its posteromedial portion, subdural electrodes over temporal and frontal cortex, and depth electrodes targeting hippocampus. Following a visual alert, subjects were presented with a pair of tones belonging to two different categories. A visual cue informed the subjects which tone to keep in mind. A 3 s retention period was followed by a tone which could be the same or different from the tone held in mind. The subjects made a same/different judgement. A total of 160 trials (80 each of 'Low' and 'High' tone retention) were presented. We measured averaged event-related potentials, carried out time-frequency analysis using wavelet transforms and examined phase-based functional connectivity.

During retention, a sustained increase (compared to rest period) in power in the beta band (15-20 Hz) was observed in the lateral part of HG. Increase in power in the gamma band (60-100 Hz) was observed in the posterior portion of superior temporal gyrus and in inferior frontal gyrus. In the hippocampus, power increase in low frequencies (less than 10 Hz) in the retention period was observed. Functional connectivity analyses revealed interactions among nodes of the auditory/frontal/hippocampal network.

The data demonstrate a network of brain regions during auditory working memory that includes auditory, frontal, and hippocampal cortex and is consistent with the network shown in our previous fMRI study (Kumar et al, J Neurosci 2016 36:4492-4505). The findings serve as a foundation for analyses of effective connectivity to test the hypothesis that the auditory cortex activity during retention is driven by the activity in inferior frontal gyrus or hippocampus.

72 The roles of NPY neurons and NPY signaling in the inferior colliculus Marina A Silveira (1), Justin D Anair (1), Nichole L Beebe (2), Laura L Burger (3), Brett R Schofield (2) and Michael T Roberts (1)
(1) Dept. of Otolaryngology-Head and Neck Surgery, University of Michigan, Ann Arbor MI.
(2) Molecular & Integrative Physiology, Univ. of Michigan, Ann Arbor, MI.
(3) Anatomy & Nuerobiology, Northeast Ohio Med. Univ., Rootstown, OH

Located in the midbrain, the inferior colliculus (IC) integrates information from numerous auditory nuclei and is an important hub for sound processing. Despite its importance, little is known about the function and molecular identity of neurons in the IC. Using a multi-faceted approach, we have identified Neuropeptide Y (NPY) as a marker for a distinct neuron class in the IC. In the NPY-hrGFP mouse line, hrGFP-positive neurons are distributed throughout the IC, and hrGFP selectively-labels IC neurons that express NPY. Immunostaining showed that NPY neurons in the IC are GABAergic (98.5% of hrGFP-positive neurons co-label with an antibody against GAD67; total NPY neurons counted: 2673). Using design-based stereology, we found that NPY neurons represent ~25% of the GABAergic neurons in the IC. To examine the physiology of NPY neurons, we targeted whole cell patch clamp recordings to hrGFP-expressing neurons in acute brain slices. These recordings demonstrated that NPY neurons exclusively exhibit a sustained firing pattern (spike frequency adaptation ratio < 2), express little Ih (sag ratio at -80mV = 0.88±0.09) and have a propensity to spontaneously fire, suggesting they might tonically release NPY in the IC. In post hoc reconstructions of recorded neurons, we found that NPY neurons have a stellate morphology and extend their dendrites across the laminar plane of the IC (n=24). NPY is a 36 amino-acid neuropeptide and one of the most abundant peptides expressed in the brain. NPY is involved in numerous physiological processes, such as synaptic transmission. Because we found that the NPY Y1 receptor is widely expressed in the IC, we next investigated what is the functional role of NPY signaling in the IC.

73 Assessing the contribution of visual speech features to audiovisual speech perception in noise

Aisling E. O'SULLIVAN(1), Aaron R. NIDIFFER(2), Edmund C. LALOR(1),(2)
(1) Trinity College Dublin(2) University of Rochester

Seeing the face of the speaker you are listening to benefits speech intelligibility - particularly in noisy situations (Sumby and Pollack, 1954). The neural mechanisms underlying this improvement in intelligibility remains unclear. Behavioral studies have found that listeners predominantly gaze at the lips of the speaker when the acoustics are noisy (Vatikiotis-Bateson et al., 1998). The use of lip information under such conditions is not surprising since the lips convey general dynamic information (which is correlated with theacoustic envelope, Chandrasekaran et al., 2009), as well as detailed articulatory movements which convey complementary information (Campbell 2008). Neuroimaging work has also found an enhancement of lip processing regions in visual cortex when the acoustics are missing (Ozker et al., 2018). Together, this suggests that the lips are an important feature of visual speech which the brain exploits to assist speech processing. Research on how the rest of the facial features contributes to speech comprehension is less clear, particularly with respect to natural speech. It has been shown that other features of the face such as jaw, eye, and head movements contribute to speech comprehension (Jiang et al., 2002; Yehia et al., 2002; Munhall et al., 2004). Yet it remains unclear whether the information that confers the improved intelligibility of noisy audiovisual speech is shared between mouth movements and other dynamic facial features or whether they carry complementary information. Here we present an experiment where we have modulated the amount of facial information available to listeners as they listen to audiovisual speech in noise (-9 dB). In particular, we have tested the effects of degrading the information available from the lips on speech comprehension - while the rest of the facial information remains intact. As well as this, we have tested if degrading all of the information except the lips affects the multisensory benefit obtained for speech in noise. Our results show that the behavioral benefits of visual speech depend on access to both visual speech dynamics and articulatory information. These results extend our understanding of the contribution of visual speech features to audiovisual speech perception.

74 Aging differentially affects the cortical representation of ramped and damped sounds

Vanessa C. Irsik (1); Ingrid S. Johnsrude (1); Björn Herrmann (1)
(1) University of Western Ontario

Encoding the amplitude envelope of speech is critical for intelligibility. Speech intelligibility declines with age, particularly in environments with background noise. This may be related, at least in part, to a change in envelope encoding. Neurons in auditory cortex of older adults synchronize more strongly with a sound's amplitude envelope compared to younger adults. Recent research in rodents indicates the shape of the amplitude envelope, such as the attack and decay, and carrier frequency may modulate this hypersensitivity. In the current EEG study, we investigate how envelope shape and sound frequency affect neural synchronization in younger and older human adults. Participants listened to 4-second 4-Hz AM narrowband noises (900-1800 Hz; 1800-3600 Hz) that varied in AM envelope shape (ramped: slow attack, sharp decay; damped: sharp attack, slow decay). Click evoked ABRs (wave I and V) did not differ between younger and older adults. However, older adults showed larger cortical responses to sound onsets relative to younger adults. Older adults also showed increased neural synchronization, independent of sound frequency, when the envelope shape was damped compared to ramped, whereas younger participants showed the opposite pattern. Although entrainment to the 4-Hz fundamental was evident in all groups, entrainment to the first harmonic was more pronounced in older compared to younger adults. Across both groups, the difference in response to damped and ramped envelopes was associated with Wave 1 latency, suggesting a link with auditory nerve function. These findings show that amplitude envelopes encoding changes with age, particularly for sounds with sharp onsets.

75 Specificity of an amygdala-prefrontal projection for integrating emotional and multisensory information in the macaque

Keshov Sharma (1), Maria Diehl (2), Julie Fudge (1), Liz Romanski (1)
(1) Dept. of Neuroscience, University of Rochester School of Medicine
(2) Psychological Sciences, Kansas State Univ., Manhattan, KS

The ventrolateral prefrontal cortex (VLPFC) is a site of multisensory integration that is highly responsive to species-specific faces and vocalizations in both monkeys and humans. Face and vocalization responsive cells have been found in the macaque VLPFC and studies indicate it receives afferents from auditory cortex, inferotemporal visual regions, and multisensory STS cortical regions. The amygdala is also highly active during the processing of facial and emotional expressions and recent studies have revealed auditory and multisensory responsive neurons in the primate amygdala. Within the amygdala, the basal nucleus is a key input to the prefrontal cortex and is massively expanded in primates. In macaques, the basal nucleus has three sub-nuclei with unique and overlapping projections to the prefrontal cortex, thereby participating in distinct but complementary microcircuits. To achieve precise insight into the potential circuit function of amygdala projections to the VLPFC, we injected bidirectional tracers into face and vocalization-responsive regions of the VLPFC and mapped retrogradely labeled cells within the amygdala. In previous electrophysiology experiments, macaques viewed or heard vocalizations, facial gestures, or audiovisual combinations of faces and vocalizations as part of a presentation task or an audiovisual working memory task. Injections of dextran-conjugated tracers were subsequently placed at VLPFC sites with a high concentration of cells responsive to species-specific vocalizations (auditory), faces (visual), or simultaneous presentations of both stimuli (multisensory). 14-21 days post-injection, animals were perfused and the brain was processed for immunocytochemical localization of labelled cells and fibers. In addition to connectivity with auditory, visual, and multisensory cortical regions in the temporal lobe, tracer injections resulted in dense concentrations of retrogradely labeled cells that were consistently found in the basal nucleus and were highly restricted to the intermediate (Bi) and magnocellular (Bmc) subdivisions of the basal nucleus. Our results establish a direct connection between the basal nucleus of the amygdala and VLPFC sites that process and integrate face and vocal information. Furthermore, this projection arises from a highly specific portion of the basal nucleus that has established connections to occipital and temporal sensory and association cortices. Our findings illustrate a direct, monosynaptic pathway by which the amygdala may participate in the processing of multisensory, social stimuli in the ventrolateral prefrontal cortex.

76 Neural correlation codes for sound identification and categorization: the contribution of sound spectrum and envelope correlation structure

Xiu Zhai (1), Mina Sadeghi (1), Fatemah Khatami (2), Fengrong He (1), Delaina Pedrick *(1), Heather Read (1), Ian Stevenson (1), Monty Escabi (1)*
(1) University of Connecticut
(2) University of California, San Francisco

In natural sounds, spectro-temporal modulations are highly structured and varied, and the envelopes are correlated both across frequencies and time. Although low-level cues, such as the sound spectrum, contribute to many auditory tasks, including sound localization and pitch perception, they are insufficient for identifying most environmental sounds. This is particularly true of natural acoustic environments where physical constraints of the environment (size, shape, and boundary materials) and source direction can dramatically shape the sound spectrum. Manipulating higher-order statistics related to the spectro-temporal modulations of sounds can dramatically influence sound recognition, and it is thus possible that the sound correlational structure is a more invariant cue than the sound spectrum for categorization tasks.
Here we tested how the sound spectrum and correlation structure of natural sounds is reflected in the firing rates and correlation structure of neural ensembles, respectively, and how each of the neural representations (place rate code vs. neural correlations) contribute to a sound identification and categorization task. Five texture sounds (crackling fire, bird chorus, crowd noise, running water and rattling snake) were delivered to unanesthetized rabbits and neural activity was obtained from the auditory midbrain (the inferior colliculus, IC) using multi-channel neural recording arrays. We demonstrate that the correlated firing between frequency organized recording sites in the IC are modulated by each of the tested sounds and these neural correlations can be used to decode and identify sound textures. Specifically, stimulus-driven spectro-temporal correlations were measured across the frequency organized recording array and a naïve Bayes classifier was applied to the ensemble correlation activities to identify the delivered sounds. The classifier was able to decode and identify these original sounds approaching near perfect accuracy (~90%). Furthermore, control tests indicate that the neural response correlation is largely invariant to changes in the sound spectrum. Preserving the modulation content of each sound while removing the sound spectrum (equalizing all sounds for 1/f power spectrum) did not have a major effect on the neural correlations or the classifier performance. However, firing rates changed substantially and the firing rate classifier performance was substantially reduced. On the other hand, removing the modulation content while preserving the original power spectrum led to a reduction in the classification accuracy for the correlation classifier. Next, we tested the neural correlation classifier on a three-sound categorization task (fire, water, and speech) with multiple exemplars (6 exemplars per category). The neural correlation structure for each sound was more similar within a category than across categories such that the classifier was able to decode and categorize the sounds with very high accuracy (>90%). These findings suggest that the coordinated firing in auditory midbrain ensembles is largely invariant to changes in the sound spectrum and thus can serve as a highly informative neural signal for identification and categorization (supported by NIDCD R01DC015138).

77 Neuronal signatures of task acquisition versus context-dependent expression in the auditory cortex

Céline Drieu (1), Ziyi Zhu (1), Srdjan Ostojic (2), Kishore Kuchibhotla (1)
(1) Johns Hopkins University
(2) Ecole Normale Supérieure, Paris, France

Performance on cognitive tasks during learning is often used to measure knowledge, yet remains controversial since such testing is susceptible to contextual factors. Here we use a novel behavioral paradigm (Kuchibhotla et al., 2019) that allows us to quantitatively dissociate knowledge acquisition from how it is demonstrably 'expressed' by changing the context of the task (presence or absence of reinforcement). We have previously shown that the dynamics of knowledge acquisition versus expression could be captured using a minimal stimulus-action association model in which knowledge of the task is acquired through reward-driven reinforcement while knowledge expression is suppressed early in learning by a contextual scaling factor that operates on the decision read-out (Kuchibhotla et al., 2019). Here, we aim to expand this model by adding an intermediate layer that integrates feedforward sensory inputs and then outputs to a decision readout layer; both this intermediate layer and the downstream decision layer are influenced by a contextual scaling factor. This intermediate layer is intended to model the role of the auditory cortex in reinforcement learning and will allow us to make testable predictions about how the auditory cortex may reflect computations associated with task acquisition versus expression. In parallel, we are combining our behavioral paradigm with two-photon calcium imaging in behaving mice to address how the excitatory neural network in the auditory cortex reflects sensorimotor learning, including both task acquisition and context-dependent expression. We monitor the activity of the same large population of pyramidal cells in layer II/III of the auditory cortex over the course of learning and analyze single cell and neuronal population activity profiles. Our preliminary data suggests that excitatory neural populations in the auditory cortex reflect the behavioral dissociation between acquisition and context-dependent expression, suggesting that both computations are indeed reflected at the level of the auditory cortex. Our work aims to develop a robust theoretical framework based on experimental data to identify cortical mechanisms underlying sensorimotor learning by dissociating acquisition of knowledge from its context-dependent expression.

78 The contribution of stimulus driven and noise correlations for neural decoding and identification of texture sounds

Xiu Zhai (1), Ian Stevenson (1), Monty Escabi (1)
(1) University of Connecticut

The amount of information conveyed by neural ensemble about a sensory stimulus is critically dependent on the correlation structure of its neural activity. On the one hand, stimulus driven correlations between neurons are often thought of as form of redundant encoding with limited encoding capacity and reduced efficiency. Alternately noise correlations, i. e., coordinated firing due to network activity unrelated to the sensory stimulus are often thought of as a form of noise that limit the classification accuracy of neural population codes. Using multi-channel neural recording arrays to record neural responses to natural sound textures in unanesthetized rabbits we demonstrate that correlated firing between frequency organized neural ensembles in the auditory midbrain (inferior colliculus) can be used to recognize sounds. To explore the contribution of stimulus driven and noise correlations for decoding the sound texture identity, we developed a noise-less and a single-trial classifier. The noiseless classifier excludes the noise correlations and thus sets an upper bound on the classification accuracy provided by the stimulus driven correlation structure. The single trial classifier, by comparison, requires that both the noise and stimulus driven correlations be taken into account. Unlike noise correlations, which are mostly unstructured (diagonalized) and vary little with the sound, stimulus driven correlations are highly stimulus dependent and their time-frequency structure was quite diverse and informative for the classification task. The noiseless classifier approached near perfect identification accuracy (average 90%) using stimulus-driven correlations only and sets an upper bound on the classification accuracy. Although the average single-trial classification performance was on average lower (70%), individual penetrations were found that approached near perfect accuracy (90%). This reduction in the classification accuracy was accurately accounted for by the noise correlations. When noise correlations are not included as part of the single-trial classifier model, single trial performance drops to near chance (20%). Furthermore, performance was highly correlated with the signal-to-noise ratio (SNR) of the neural correlations: classifier performance was higher for recording locations with higher SNR. Thus, unlike previous studies which have proposed that correlated firing is generally detrimental, these findings suggest that stimulus-driven correlations can be quite informative for sound identification whereas noise correlations limit the classification performance (supported by NIDCD R01DC015138).

79 A corticothalamic circuit for motor modulation of auditory processing

Kameron K. Clayton (1,3), Ross S. Williamson (2,3), Gen-Ichi Tasaka (4), Adi Mizrahi (4), Troy A. Hackett (5), Daniel B. Polley (1,2,3).

(1)Program in Speech and Hearing Biosci. and Technology, Div. of Med. Sci.,Harvard Medical School

(2) Dept. of Otolaryngology, Harvard Med. Sch.

(3) Eaton-Peabody Labs, Massachusetts Eye and Ear

(4) The Edmond and Lily Safra Ctr. for Brain Sciences, The Hebrew Univ. of Jerusalem

(5) Dept. of Hearing and Speech Sci., Vanderbilt Univ.

Auditory cortex (ACtx) pyramidal neurons are suppressed during movement, which reduces sound-evoked activity and behavioral detection of faint sounds. Movement-related suppression of ACtx pyramidal neurons is thought to arise through projections from the basal forebrain and secondary motor cortex (M2) that engage local GABA circuits within the ACtx. While some fraction of pyramidal neuron suppression reflects monosynaptic connections from M2 onto GABA neurons, the influence of neuromodulatory inputs are often brokered by intermediaries in layer (L) 1 or L6 that directly adjust local excitability and tuning. Ntsr1-expressing layer 6 corticothalamic (L6 CT) neurons regulate sensory gain throughout the column by recruiting specialized networks of fast-spiking inhibitory neurons, suggesting that L6 CTs could be activated by motor preparatory signals to drive local GABA networks and suppress excitatory activity. To test this prediction, we used 2-photon calcium imaging to measure activity from L6 CT neurons or L2/3 Thy1+ pyramidal neurons while mice performed a simple task that isolated the contribution of movement, sensory, and reward-related inputs. We confirmed reports that self-generated movements such as licking or running suppressed spontaneous and sound-evoked activity in L2/3 pyramidal neurons. By contrast, L6 CTs were activated immediately prior to and during movement onset. Unlike L2/3 pyramidal neurons, sound-evoked responses in L6 CTs were not attenuated during movement, and were often enhanced. Pseudo-typed rabies tracing identified substantial numbers of long-range monosynaptic inputs onto L6 CT neurons from cholinergic and non-cholinergic neurons at the border of globus pallidus and the basal forebrain. Few input neurons were identified in M2. These findings suggest that L6 CTs may act as an intermediary between long-range motor inputs from the basal forebrain and basal ganglia, but that M2 may bypass L6 CTs and connect directly onto local GABA cells within ACtx. To better identify the sequence of ACtx neural activation during movement with millisecond precision, our ongoing experiments rely on electrophysiological recordings from optogenetically identified L6 CT neurons as well as local regular- and fast-spiking neurons.

80 Synaptic integration and sound processing by VIP neurons in the inferior colliculus of mice

David Goyer (1), Marina A Silveira (1), Alexander P George (1), Nichole L Beebe (2), Brett R Schofield (2), Michael T Roberts (1)
(1) Kresge Hearing Research Institute, Department of Otolaryngology – Head and Neck Surgery, University of Michigan, Ann Arbor, Michigan 48109
(2) Department of Anatomy and Neurobiology, Northeast Ohio Medical University, Rootstown, Ohio 44272

The central nucleus of the inferior colliculus (ICc) is the hub of the ascending auditory system, as it is a nearly obligatory processing center for the output of the auditory brainstem. To better understand how sounds are processed in the ICc, it is important to identify the classes of neurons that make up the ICc and determine how they function within neural circuits. By using a combination of genetic, anatomical, and physiological methods, we recently identified a novel class of stellate cells that are labeled in Vasoactive Intestinal Peptide (VIP)-IRES-Cre mice. VIP neurons in the ICc are glutamatergic, have a sustained firing pattern (214 / 237), have a stellate morphology, represent ~ 20% of stellate cells in the ICc, and 94% (81 / 86) have spiny dendrites. Via axonal tract tracing studies, we found that VIP neurons project to auditory thalamus, auditory brainstem, the periaqueductal gray, and superior colliculus. Using Channelrhodopsin assisted circuit mapping (CRACM), we found that VIP neurons receive input from the contralateral IC (n = 39) and the contralateral DCN (n = 25). Commissural inputs could be excitatory or inhibitory, or a combination of both. Excitatory commissural inputs were mediated by AMPA and NMDA receptors, while inhibitory inputs were mediated by GABAA receptors. EPSPs evoked by optical stimulation of DCN afferents were excitatory, surprisingly slow (halfwidth: 15.8 ± 9.8 ms) and had no NMDA receptor contribution. Activation of DCN afferents also elicited feedforward inhibition (FFI), which limited EPSP duration (n = 5). This FFI was blocked by tetrodotoxin, confirming it results from disynaptic transmission.
Having identified VIP neurons as a distinct neuron type in the IC, we are now probing their functional role in sound processing. In in vivo extracellular recordings we found that VIP neurons exhibit narrow tuning curves and are only weakly driven by sinusoidal-amplitude modulated (SAM) tones. Yet, VIP neurons respond well to broadband and SAM noise, indicating that they might need to integrate inputs over a range of frequencies to be driven faithfully. This is consistent with their stellate morphology in which their dendrites cross multiple isofrequency laminae. Using two-color CRACM in vitro, we also are working to identify how inputs from the DCN and contralateral IC combine with FFI to shape the output of VIP neurons. These experiments are a critical step toward defining how ICc neurons integrate diverse streams of inputs and influence sound processing in the IC."

81 What white matter plasticity can tell us about the associations between tinnitus and hearing loss

Rafay A. Khan (1), Sara A. Schmidt (1), Yihsin Tai (1), Somayeh Shahsavarani (1), Fatima T. Husain (1)

(1) University of Illinois at Urbana-Champaign

Tinnitus, the perception of sound in the absence of an external source, has been attributed to changes in both the periphery (e.g. hearing loss) and the cortex. It is unclear, however, what specific neuroanatomical and functional changes co-occur with tinnitus. More confusing still is the nature of the association between hearing loss and tinnitus – most tinnitus patients have decreased hearing sensitivity, but half of those with hearing loss do not have tinnitus. The goal of the current study was to parse out the relationship between hearing loss and tinnitus by examining white matter (WM) tracts in the brain. Diffusion tensor imaging (DTI) data were collected from 76 participants across 4 groups – controls with normal hearing (n=17), controls with hearing loss (n=11), tinnitus subjects with normal hearing (n=11) and tinnitus subjects with hearing loss (n=37). Diffusion was measured along 60 directions using a 3T Siemens Prisma scanner. Fractional anisotropy (FA) analysis was conducted using FSL FMRIB and TBSS libraries. Whole brain analysis focusing on the two tinnitus groups revealed six major tracts that showed diminished integrity in the hearing loss group compared to the normal hearing group, using a FWE correction of $p<0.05$ - the left anterior thalamic radiation (ATR), bilateral anterior corona radiata (ACR), bilateral inferior longitudinal fasciculi (IF-OF), right uncincate fasciculus, right inferior longitudinal fasciculus, and bilateral superior longitudinal fasciculi (SLF). To parse out the association of observed changes with tinnitus and hearing loss, supplementary ROI analysis was conducted, with individual FA values being extracted from all 4 groups from each of the regions described above. FA values in the left ATR, ACR, IF-OF, and SLF showed an inverse relationship with pure-tone average hearing loss (measured at 2,4,6,8 kHz frequencies), suggesting that these regions may be associated with the degree of hearing loss, regardless of tinnitus status. No strong associations were seen with the scores of Tinnitus Functional Index, which may be attributed to the relative homogeneity of tinnitus severity amongst our participants. With the collection of additional data, we hope to elucidate the neural correlates of these two associated disorders.

82 Diverse brain regions targeting layer 1 interneuron subtypes in auditory cortex

Carolyn G. Sweeney (1,2), Ana C. Castro (1), Benjamin M. Glickman (1), Jacob D. McLennan (1,3), Emma He (1,3), Anne E. Takesian (1,2)
(1) Massachusetts Eye and Ear Infirmary, Boston, MA
(2) Otolaryngology, Harvard Medical School, Boston, MA
(3) Harvard University, Cambridge, MA

The primary auditory cortex (A1) receives sensory input from the auditory thalamus as well as neuromodulatory centers throughout the brain. Neuromodulatory projections powerfully filter and modify ascending auditory signals from thalamus, thereby influencing sound perception and sound-driven behaviors. The convergence of ascending sensory and neuromodulatory signals in A1 can induce long-lasting changes in cortical sound responses that may underlie auditory learning. Recent work from our laboratory and others implicates Layer 1 (L1) of A1 as a key site for integrating both sensory signals and information about behavioral state and outcome. The interneurons that populate L1 are composed of multiple subgroups, characterized by the selective expression of distinct molecular markers, such as vasoactive intestinal peptide (VIP), neuron-derived neurotrophic factor (NDNF) and gamma synuclein (SNCG). Our recent results demonstrate that these subclasses of cortical L1 interneurons differentially receive input from thalamic nuclei. Further, they differentially express receptors for neuromodulators such as acetylcholine, serotonin, and corticosteroids, suggesting that distinct brain regions may preferentially innervate these interneuron subtypes. Our ongoing work using 2-photon calcium imaging is revealing parallel differences in the in vivo activity patterns of these interneuron subclasses in response to both a range of sound and other behaviorally relevant stimuli. Together, these studies will expand upon our current understanding of the anatomical and functional diversity of L1 circuits in A1 for conveying distinct auditory and neuromodulatory information.

83 Intracranially recorded neural activity in auditory cortex elicited by simple sounds and during naturalistic verbal interactions in children

Ariane E Rhone (1) Mitchell Steinschneider (2) Beau F Snoad (1) Kirill V Nourski (1) Christopher K Kovach (1) Brian J Dlouhy (1)
(1) University of Iowa
(2) Albert Einstein College of Medicine

Neurosurgical interventions for remediation of medically intractable epilepsy in children have become a viable clinical option in pediatric patients. A companion presentation (Steinschneider et al, APAN 2019) examines basic response properties of auditory cortex on Heschl's gyrus. Here, we examine neural activity recorded from lateral superior temporal gyrus (STG) and other fronto-temporo-parietal areas. All studies were approved by the NIH and the University of Iowa Institutional Review Board. Informed consent was provided by the children's parents or legal guardians. Verbal or written assent was obtained from the children. Subdural grid electrodes were placed over the lateral STG in three right-handed subjects (ages 9, 13, and 14). One subject had left and two had right hemisphere coverage. Analysis focused on local field potentials and event-related high gamma power (70-150 Hz). Stimuli included a wide variety of sounds including tones, click trains, speech and environmental sounds. Additionally, children engaged in a question-answer dialog based on that used previously (Nourski et al, 2016, Front Hum Neurosci 10:202) and a structured version of the children's card game "Go Fish." Neural activity elicited by sounds was maximal on the lateral STG near the transverse temporal sulcus. Activity was seen for all sound types, though speech generally elicited more widespread responses than pure tones and click trains. Responses to human vocalizations and environmental sounds (Belin et al, Nature 2000, 403:309-12) were similar in magnitude. Consonant-vowel syllables elicited local field potentials that differed between voiced and unvoiced consonants (5 ms and 40 ms voice onset time, respectively). Naturalistic interactions were characterized by a widespread activation within and beyond auditory cortex, including prominent responses in parietal areas when the subjects heard number words.We conclude that responses to isolated word and nonword stimuli on the lateral STG are similar to those seen in adults. Furthermore, preliminary results provide proof of concept that naturalistic interactive tasks are feasible in children undergoing invasive monitoring for treatment of their medically intractable epilepsy and can be used to probe auditory cortical function.

84 Delayed tone-discrimination in the macaque monkey is tone intensity-invariant but improves linearly with tone duration

Tobias Teichert (1)

(1) Department of Psychiatry and Bioengineering, University of Pittsburgh

Auditory information is briefly stored in a passive sensory buffer (echoic memory) for comparison with subsequent sounds. The neural substrate of echoic memory is unclear, but given the sensory nature of echoic memory, it is commonly assumed to reside in early sensory regions such as primary auditory cortex (A1). However, it is not known if echoic memory is affected by the same stimulus properties that are known to affect neural responses in A1 of animal model systems such as the macaque monkey. In particular, it is not known if echoic memory the monkey is affected by tone intensity which increases response amplitudes and widens receptive fields in A1, or by tone duration which has only minor effects on the mostly phasic responses in A1.

Two macaque monkeys were trained to release a lever if and when a series of identical pure tone pips was interrupted by a deviant pip of different tonal frequency. Across different trials, the pips were presented at one of 5 intensities (40, 50, 60, 70 or 80dB SPL) and one of six durations (25, 50, 75, 100, 150, or 200 ms). Inter-stimulus intervals were kept between 500 and 1000 ms, a range in which task performance was shown to depend mostly on information in echoic memory. EEG responses were recorded from arrays of up to 32 chronically implanted cranial EEG electrodes. Echoic memory function was quantified as the slope of the psychometric function relating the frequency-difference between standard and target tone to lever release probability.

Except for the softest tones, echoic memory was invariant across a wide range of stimulus intensities. In contrast, echoic memory improved significantly and substantially as a function of tone durations. The improvement was approximately linear across the range of presented durations. Follow-up experiments suggested that the effect was driven by more accurate encoding of information into echoic memory rather than prolonged maintenance. The effect of tone intensity and duration on neural responses was quantified via auditory evoked EEG potentials. As expected, EEG potentials increased with intensity. In contrast, none of the evoked potentials was modulated by tone duration. These findings highlight an intriguing double-dissociation between echoic memory function and neural responses.
Our findings provide two novel insights into echoic memory function in the macaque: (1) Echoic memory is largely indifferent to tone intensity despite its well-known effect on neural response amplitude and receptive field width in A1. It remains to be tested how this intensity-invariance is implemented at the neural level. (2) Encoding of information into echoic memory improves with tone duration suggesting a temporal integration window above 200 ms. It remains to be tested if and how temporal integration is related to the relatively small fraction of neurons in A1 that exhibit sustained responses to their preferred stimulus, and how information contained in sustained firing is integrated over time. We will discuss short-term pre-synaptic depression as one candidate mechanism of echoic memory that can account for temporal integration of stimulus information."

85 **Cortical activation in a mouse model of the auditory brainstem implant** Vivek Kanumuri* (1,2), Angela Zhu* (1,2,3), Amalia Davis (1,2), Ahad Qureshi (1,2), Stephen McInturff (1,2), Osama Tarabichi (1,2), Nicolas Vachicouras (4), Kameron Klayton (1,2), Stephanie Lacour (4), M. Christian Brown (1,2), Daniel Polley (1,2), Daniel Lee# (1,2), Anne Takesian# (1,2)
(1) Massachusetts Eye and Ear Infirmary
(2) Harvard Medical School
(3) Howard Hughes Medical Institute
(4) Ecole Polytechnique Federale de Lausanne

Auditory brainstem implants (ABIs) are neuroprosthetic devices that provide auditory input to profoundly deaf patients who are not candidates for cochlear implants due to a damaged or absent auditory nerve. However, auditory outcomes in patients with ABIs are poor relative to cochlear implants. Efforts to improve current ABI technology are challenged by a lack of understanding of how ABIs recruit the auditory system, particularly the auditory cortex. Here, we developed a unique mouse model that enables imaging of auditory cortex neuron activity in response to both ABI stimulation and sound input. Mice are chronically implanted with a flexible electrode ABI before receiving a cranial window and GCaMP6s viral injection. Using two-photon calcium imaging, we imaged L2/3 auditory cortex neurons in awake mice and compared their activity in response to either broadband frequency noise bursts or an electrical ABI impulse delivered to the cochlear nucleus. Our preliminary data suggests that the subset of auditory cortex neurons that show activity in respond to noise bursts are also activated by ABI electrical impulses. To then ask whether these animals are able to achieve perceptual saliency with the ABI electrical impulse, we also trained animals on an auditory Go/No go behavioral task for a water reward. Animals were trained to detect a broadband frequency 70 dB acoustic noise burst or ABI electrical input. Examining which cortical neurons are activated by sound vs. ABI-evoked sound representations may offer insights into improving ABI design, and ultimately lead to better outcomes in patients who must learn to interpret sound signals through these implants.

86 Dissociating the role of cholinergic signaling in task acquisition versus expression during sensorimotor learning

(1) Sarah Elnozahy (2) Tara Raam (3) Aaron Wang (4) Srdjan Ostojic (5) Kishore V. Kuchibhotla

(1) Johns Hopkins University
(2) Johns Hopkins University
(3) Johns Hopkins University
(4) École Normale Supérieure
(5) Johns Hopkins University

Performance on cognitive tasks during learning involves both the acquisition of task contingencies (e.g. stimulus-action associations), and the correct expression of that underlying knowledge in the appropriate context. Here, we use a novel behavioral paradigm (Kuchibhotla et al., 2019) that allows us to quantitatively dissociate knowledge acquisition from how it is demonstrably 'expressed' by changing the context of the task (presence or absence of reinforcement). We are able to dissociate the acquisition and expression of task knowledge by testing the animal in two, interleaved, contexts: a "reinforced" context, which includes reward, and a "probe" context, in which no reward is delivered. We constructed a network model to determine how stimulus-action associations can be acquired versus expressed at different rates. Our model suggests that the observed behavioral dissociation in learning occurs due to a contextual scaling factor, which biases the decision readout. Here, we test the hypothesis that optimally tuned cholinergic neuromodulation is critical for effective behavioral expression of learned knowledge.
To do so, we considered whether tonic cholinergic signaling from the basal forebrain, which projects broadly to both sensory and decision-related circuits, may play a permissive role in behavioral expression. We specifically test whether an excess of tonic cholinergic neuromodulation is responsible for suppressing task relevant information in the 'reinforced' context early in learning. We virally express eNhPR3.0 in cholinergic neurons in the basal forebrain of ChAT-cre mice . Using optogenetics, we suppress the basal forebrain in a block-based manner at a time-point early in learning where mice perform poorly in the reinforced context (e.g. lick to both target and foil tones) but at expert levels in the probe context (e.g. lick only to target tone). Preliminary experiments suggest that bilateral suppression of cholinergic activity partially "closes the gap" between performance in the probe and reinforced contexts in a rapid and reversible fashion. These data suggest that optimally tuned cholinergic neuromodulation is critical for task expression early in learning. We are monitoring activity of cholinergic axonal projections to the auditory cortex using two-photon calcium imaging to determine the tonic and phasic activity patterns of cholinergic activity during sensorimotor learning. We hope to identify the role of cholinergic signaling in modulating behavioral expression as distinct from task acquisition."

87 Deep Neural Networks as Models of Real-World Human Sound Localization

Andrew Francl (1) Josh McDermott (1,2)
(1) MIT Brain and Cognitive Sciences
(2) Harvard-MIT Speech and Hearing Bioscience and Technology

The ability to localize a sound source by listening is a core component of audition, and has been a focus of hearing research for over a century. Sound localization has traditionally been studied using simple sounds and listening conditions, such as single noise bursts or tones in anechoic environments. However, in everyday life we localize sounds in environments with multiple sound sources, background noise, and room reverberation. At present we lack models that can explain these everyday abilities.

Recent engineering advances have led to artificial neural network models that perform at human levels for many perceptual tasks. Such network models are optimized to extract cues from the input that best support performance of the trained task. As a result, a trained model can reveal characteristics of near-optimal performance, and can provide hypotheses for biological systems that solve the same task. We utilized this approach to build a model that localizes sound sources in noisy reverberant environments from binaural audio. Following optimization, the model accurately localized natural sounds in 3D space amid background noise and reverberation. We then simulated a large set of classic psychoacoustic experiments on the model. Despite having no previous exposure to the tone and noise stimuli nor the anechoic environment used in the experiments, the model qualitatively replicated a number of classic behavioral effects, including the frequency-dependent use of interaural time differences (ITDs), the use of envelope ITDs at high carrier frequencies, increased localization errors away from the midline, and better localization with increasing stimulus bandwidth. Contrary to the textbook account of binaural hearing but consistent with recent human data, the model was sensitive to interaural level differences (ILDs) at both low and high frequencies. The results suggest that many human sound localization behaviors may be understood simply as a consequence of optimization for real-world localization.

88 Phasic arousal suppresses suboptimal decision biases in mice and humans

Jan Willem de Gee (1,2,3,4), Konstantinos Tsetsos (1), Lars Schwabe (5), Anne E Urai (1,2,6), David A McCormick (7,8), Matthew J McGinley (3,4,8), Tobias H Donner (1,2,9)

1 Department of Neurophysiology and Pathophysiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
2 Department of Psychology, University of Amsterdam, Amsterdam, Netherlands;
3 Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA;
4 Jan and Dan Duncan Neurological Research Institute, Texas Children's Hospital, Houston, TX, USA;
5 Department of Cognitive Psychology, Institute of Psychology, University of Hamburg, Germany;
6 Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA; 7Institute of Neuroscience, University of Oregon, OR, USA;
8Department of Neuroscience, Yale University, New Haven, CT, USA;
9Amsterdam Brain & Cognition, University of Amsterdam, Amsterdam, Netherlands.

Decisions under uncertainty entail an accumulation of ambiguous evidence supporting different choice alternatives. The brain's arousal systems are rapidly recruited during such decisions. But how do the rapid ("phasic") arousal boosts affect decision-making? We here established a principle of the function of phasic arousal in decision-making, which generalizes across species (humans and mice) and behavioral tasks (from perceptual to memory-based and numerical decisions): suppressing maladaptive biases in the accumulation of evidence leading up to choice.

We exploited that pupil dilation indexes cortical arousal state as well as response of the noradrenergic locus coeruleus in humans, monkeys and mice. We recorded the pupil diameter of 20 humans and 5 mice during a difficult auditory go/no-go detection task. Humans responded with a button press, mice by licking for sugar water reward. In addition, 15 human subjects performed a forced-choice decision task based on identical stimuli under systematic manipulations of target probabilities, 54 human subjects performed a memory-based decision task, and 37 human subjects performed a basic laboratory task model of value-based stock market decisions.

In mice and humans, task-evoked pupil responses occurred early during decision formation, even on trials without any motor response, and predicted a suppression of a suboptimal conservative choice bias. Drift diffusion modeling revealed that the bias reduction was due to a selective interaction with the evidence accumulation process, rather than a shift in starting point. We showed that, within the same subjects, phasic arousal flexibly reduces both conservative and liberal accumulation biases in a context-dependent manner. The same pupil-linked suppression of evidence accumulation bias also when evidence is accumulated from memory. Finally, by comparing a leaky selective integration model to other accumulation-to-bound models, we found a similar reduction in evidence accumulation bias towards risk-seeking, a higher-level form of human bias widely known in behavioral economics.

Our findings point to a precise, yet broadly generalized, role for global arousal state of the brain in decision making in the face of uncertainty. Our results indicate that pupil-linked phasic arousal suppresses choice biases in evidence accumulation across species and across domains of decision-making, ranging from decisions based on low-level perceptual evidence, to evidence sampled from memory, to high-level numerical evidence. In conclusion, phasic arousal calibrates a key computation during decision-making.

89 High Frequency Time Locking in Human Auditory Cortex to Continuous Speech

Joshua P. Kulasingham (1), Christian Brodbeck (1), Alessandro Presacco (1), Stefanie E. Kuchinsky (2), Samira Anderson (1), Jonathan Z. Simon (1)
(1) University of Maryland, College Park
(2) Walter Reed National Military Medical Center

The neural processing of natural sounds, such as speech, changes along the ascending auditory pathway, and is often characterized by a progressive reduction in representative frequencies. For instance, the well-known frequency-following response (FFR) of the auditory midbrain, measured with electroencephalography (EEG), is dominated by frequencies from ~ 100 Hz to several hundred Hz, and time-locks to acoustic features (waveform and envelope) at those rates. In contrast, cortical responses, whether measured by EEG or magnetoencephalography (MEG), are thought to be characterized by frequencies of a few Hz to a few tens of Hz, time locking to acoustic envelope features at those rates. In this study we show that this separation by frequency is overly simplistic, even for non-invasive electrophysiological recordings in humans. Using MEG we investigate high-frequency responses (80-300 Hz) to continuous speech using neural source-localized reverse correlation, whose kernels are called temporal response functions (TRFs). Continuous speech stimuli were presented to 40 subjects (17 younger, 23 older) with clinically normal hearing and their MEG responses were analyzed in the 80-300 Hz band. Consistent with the insensitivity of MEG to many subcortical structures, the spatiotemporal profile of these response components indicate a purely cortical origin with ~40 ms peak latency and a right hemisphere bias. TRF analysis was performed using two separate aspects of the speech stimuli: a) the 80-300 Hz band of the speech waveform itself, and b) the 80-300 Hz envelope of the high frequency (300-4000 Hz) band of the speech stimulus. Both of these aspects contributed to the TRF, with the envelope dominating the response. Age-related differences were also analyzed to investigate a reversal previously seen along the ascending auditory pathway, whereby older listeners have weaker midbrain FFR responses than younger listeners, but, paradoxically, have stronger low frequency cortical responses. In contrast to these earlier results, this study did not find clear age-related magnitude differences in high frequency cortical responses. Together, these results suggest that the traditional EEG-measured FFR has distinct and separate contributions from both subcortical and cortical sources. The cortical responses at FFR-like frequencies share properties with both midbrain responses at the same frequencies and cortical responses at much lower frequencies.

90 Comparison of spatial and talker selective attention in a multi-talker scenario

Winko W. An (1), Abigail Noyce (3), Alexander Pei (1,4), Barbara G. Shinn-Cunningham (1, 2, 4)
(1) Department of Electrical and Computer Engineering, Carnegie Mellon University
(2) Neuroscience Institute, Carnegie Mellon University
(3) Department of Psychological and Brain Sciences, Boston University
(4) Department of Biomedical Engineering, Boston University

Introduction
People exploit spatial cues (e.g. azimuth, elevation) and/or talker-specific cues (e.g. pitch, timber) to sustain a conversation in a multi-talker scenario. There is growing interest in understanding how the human brain focuses on an auditory object when different attentional cues are being used. The current fMRI study sought to investigate the differences and similarities in brain activity pattern when we attend to a specific direction, or to a specific talker for the same physical mixture of sounds.

Method
19 young adults participated in this study. The auditory stimuli comprised the syllables Ba/Da/Ga spoken by 5 distinguishable talkers, and played from 5 possible directions (left/right 90˚/30˚, center). The experiment consisted of 21 conditions (36 trials each) that differed in the type of task (spatial/talker/no attention) and the gender/direction of the target. For each trial, the subjects were given a visual cue and an auditory cue before the onset of a 4-syllable mixture. The cues conveyed information about the type of task and the direction/talker of the target. For a spatial- or a talker-attention trial, subjects were asked to report the syllable from the target direction/talker in the mixture. In control trials, subjects were asked to ignore the stimuli. fMRI data, recorded throughout the experiment, were pre-processed and analysed using a general linear model whose regressors matched the form of attention. A one-sample t-test on the subject-level t-statistics was used to make group-level inferences (alpha=0.01, FDR corrected). The performance of subjects, in the form of their percent accuracy, was also compared between spatial and talker attention tasks using a student t-test.

Results
Attending to a specific talker (97.79% correct) proved to be a much easier task than attending to a direction (89.14% correct, p=0.0001). The superior and inferior part of the precentral sulcus (sPCS, iPCS), the circular sulcus of the insula, the intraparietal sulcus (IPS) and the anterior part of the cingulate cortex (ACC) showed stronger responses when attention was required compared to the passive condition. Spatial attention elicited significantly more activation than talker attention in all the aforementioned regions except iPCS. Talker attention induced stronger activation in the triangular part of the inferior frontal gyrus (trIFG) than spatial attention. The activation of the default mode network (DMN) was more prominent when in the passive condition, and was stronger during talker than spatial attention.

Conclusion
This study revealed an attention network that is shared by spatial- and talker-specific attention. The behavioural data and the DMN activation also show that in a multi-talker

scenario, a talker-specific cue is more effective and easier to use than a spatial cue. This difference in task difficulty could explain the fact that most of the brain regions in the shared attention network were activated more strongly during spatial attention than talker attention, pointing to the need for further investigation into these differences.

91 Effects of task and arousal level on the processing of peri-threshold tones investigated with MEG, EEG, and pupillometry

Laura Doll (1), Andrew R. Dykstra (2), Alexander Gutschalk (1)
(1) Dept. of Neurol., Ruprecht-Karls-Universität Heidelberg, Heidelberg, Germany
(2) Dept. of Biomed. Engin., Univ. of Miami, Coral Gables, FL

Conscious perception of weak stimuli is state-dependent and likely influenced by selective attention and arousal level. We studied these factors using a multi-block tone-in-noise detection experiment. In blocks 1 and 3, participants detected weak but supra-threshold amplitude modulation (AM) of continuous white noise; in block 2, they detected peri-threshold tones embedded in the noise. Cortical activity was measured with simultaneous MEG/EEG, and pupil dilation was used as a proxy for locus coeruleus activity (related to arousal).

Mean hit rate for tone-in-noise detection in block 2 across listeners (N=11) was 41% (range 27-52%); mean hit rate for AM detection (blocks 1 and 3) was 74% (range 42-96%). Hit rate was significantly correlated with pre-stimulus pupil size. None of the listeners noted the presence of the peri-threshold tones in block 1; five did in block 3. In block 2, auditory cortex activity between 150 and 250 ms was present irrespective of tone detection, but much larger for detected tones. No such activity was observed for the same tones when they were task-irrelevant (blocks 1 and 3). Later (400-600 ms) activity in posterior cingulate cortex was observed for hits but neither for misses nor for non-target conditions (for both, peri-threshold tones and AM). Significant transient pupil dilation was only observed for targets and was larger for hits than misses.

These results are consistent with roles of arousal and selective attention in biasing detection of peri- threshold tones: (1) Higher arousal levels as indexed by pupillometry were associated with higher detection probability. (2) Significant AC activity was only evoked by peri-threshold tones when they were task-relevant. This AC activity may reflect conscious perception of the tones. However, this conclusion is limited by the post-hoc report of tone detection in block 3 by a subgroup of participants, which was not paralleled by AC activity in the average response. Enhanced AC and pupil responses for missed peri-threshold tones in block 2 may either be related to a conservative response criterion or to attentional effects operating on non-perceived stimuli.

92 Graded control of pupil dilation and cortical neuromodulation using selective and parametric stimulation of the Vagus Nerve

Zakir Mridha (1), Jan Willem de Gee (1), Yanchen Sh (1)i, Rayan Alkashgari (2), Justin Williams (2), Aaron Suminski (2), Matt Ward (3), Wenhao Zhang (1), and Matthew McGinley (1)
(1) Baylor College of Medicine
(2) University of Wisconsin
(3) Purdue University

The vagus nerve relays information about brain state to the body. Vagus nerve stimulation (VNS) is thought to 'back fire' neuromodulatory centers (such as locus coeruleus), releasing neuromodulators (such as norepinephrine) throughout the brain. The neuromodulatory effects of VNS are thought to mediate its clinical benefits, in for example the treatment for refractory epilepsy, tinnitus, or depression. Furthermore, VNS enhances auditory learning in healthy individuals, hypothetically by boosting cortical plasticity via the same neuromodulators (Engineer et al., 2015). A major challenge in using VNS, for therapeutic purposes or cognitive enhancement, is that there is no known readout of nerve engagement or subsequent neuromodulatory impact. As a result, stimulation parameters are chosen and optimized, largely through trial-and-error and feedback from patients about symptoms and side effects. We have previously shown that the size of the pupil tracks neuromodulatory brain state and its influence on auditory physiology and behavior (McGinley et al., 2015; Reimer et al., 2016).
Here, we developed a VNS preparation for awake, head-fixed mice and test if pupil dilation can serve as a biosensor of VNS and associated cortical neuromodulation. We adapted an implanted cuff design from prior work in rats (Ward et al., 2015). Stimulation via our cuff is well-tolerated by mice for up to several months. We performed an extensive search across a VNS parameter space of 4 pulse widths (0.1-0.8 ms), 5 amplitudes (0.1-0.9 mA), and 3 rates (5-20 Hz; 10 s trains), while monitoring pupil size and other eye and facial movements. We found consistent pupil dilation that parametrically increased with increasing pulse width, amplitudes or rate. Experiments with promiximal (or proximal and distal) cut of the nerve confirm that the pupil dilation results from selective activation of the vagus nerve. Using two-photon imaging of axons in auditory cortex, we observed that cortical neuromodulation was phasically boosted during VNS, and then decayed back to a stable baseline. We also found that care with grounding and current spread is necessary to avoid major off target effects such as small phase-locked eye movements and further pupil dilation. Taken together, our results provide a foundation for carefully controlled VNS, and pupil dilation as its readout, for the enhancement of auditory learning and other applications requiring closed-loop, graded control of brain state.
References: McGinley et al. (2015), Neuron, 87. Reimer, McGinley, et. al. (2016), Nature communications, 7. Engineer et al. (2015), Brain Stimulation, 8. Ward et al. (2015), IEEE Trans Neural Syst Rehabil Eng, 23.

93 Characterization of modularity in the lateral cortex of the mouse inferior colliculus using a combination of optogenetic circuit mapping and in vivo two-photon imaging

Baher A. Ibrahim (1,2) and Daniel A. Llano (1,2,3)
(1) Department of Molecular and Integrative Physiology, University of Illinois at Urbana-Champaign, IL, USA.
(2) Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, IL, USA.
(3) Neuroscience Program, University of Illinois at Urbana-Champaign, IL, USA.

The inferior colliculus (IC) is a critical midbrain structure for the processing of auditory stimuli. The IC is a hub that permits widespread convergence of both bottom-up and top-down projections involving auditory, somatosensory, visual, motor and arousal-related brain regions. One of the non-lemniscal divisions of the IC, the lateral cortex (LC), contains periodic modules of GABAergic cells and terminals which stain strongly for a range of metabolic markers. Anatomically, auditory inputs from the auditory cortex or central nucleus of the IC strongly avoid these inhibitory modules and instead form dense projections to the matrix areas that surround the modules. In addition, these modules receive direct inputs from the somatosensory brain regions. On cell type, GABAergic cells in the modules, appears to integrate information between the modules and matrix and therefore may be critical to multisensory integration. However, there is no clear mechanism about the function of these inhibitory modules in sensory processing. Here we show using laser-assisted mapping that AC terminals in the LC made monosynaptic connections with all LC neurons with the exception of GABAergic cells in the modules, which we previously have shown to be the only cell type in the LC to receive substantial intrinsic cross-module inputs. In addition, two-photon imaging was used here to characterize the functional activity of the GABAergic and nonGABAergic cells inside and outside the modules). We observed strong tone-responsiveness in the LC, with a broad array of tuning widths. These data suggest that module/matrix organization of the lateral cortex has the capacity to process auditory stimuli while being modulated by auditory cortical projections.

94 Characterizing the nonlinear encoding of speech in the human auditory cortex

Menoua Keshishian
(1), Hassan Akbari (1), Bahar Khalighinejad (1), Jose L Herrero (2), Ashesh D Mehta (3), Nima Mesgarani (1)
(1) Columbia University
(2) Feinstein Institute for Medical Research
(3) Hofstra Northwell School of Medicine

There is a growing interest in characterizing the response properties of sensory neurons under natural stimulus conditions. The majority of previous studies have used linear models to relate the acoustic features of sound to neural responses. Linear models, however, cannot capture the inherent non-linearity of the processes in the brain. Recent advancements in machine learning and computational power have allowed us to utilize deep learning methods in a large variety of tasks. We investigate the utility of deep neural network models to predict neural responses to speech in human auditory cortex, with the goal of analyzing the learned networks to gain insight into the nonlinear mechanisms of the brain. The neural responses were recorded from the transverse and the superior temporal gyrus of five patients undergoing surgery for the treatment of epilepsy, as they listened to continuous speech. As deep neural networks (DNNs) have shown great promise in capturing non-linear relationships, we trained a convolutional neural network (CNN) with a non-linearity in each layer using the time-frequency representation of the stimulus as the input and the envelope of the high-gamma activity of the neural responses as the output of the model, to study the effect of artificial neural networks.
In comparison to the STRFs, the predicted responses from the neural networks had a higher correlation with the original responses. On average, using CNNs improved performance by 25%. To interpret the nonlinear function that the network applies to the stimulus, we analyze the linear equivalent of the function, at each time point. As a result, we observe three general classes of nonlinear behavior implemented by the network: gain change, latency shift, and shape diversity. The latency shift can be interpreted as the network holding on to a response captured by the STRF or in other words temporal integration. Finally, we quantify these properties for all electrodes and try to explain the prediction improvement gained from using the CNN model, through these simple parameters. Furthermore, we studied the relation between these parameters and the electrodes' anatomical locations and other encoding properties.

95 Auditory Attentional Modulation in Cochlear Implant Users

Jason Geller (12), Ann Holmes (3), Kyung-Joong Kim(3) Subong Kim(3), Inyong Choi(3)
(1) Department of Psychology and Brain Sciences, University of Iowa, Iowa City, IA, USA
(2) Department of Otolaryngology-Head and Neck Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA, USA
(3) Department of Communication Sciences and Disorders, University of Iowa, Iowa City, IA, USA

Conversations often take place in sub-optimal (noisy) environments. In order to accurately perceive speech in noise (SiN), selective attention is needed, which involves attending to a task-relevant sound source while avoiding distraction from concurrent sounds. In hearing impaired listeners, the most commonly cited complaint is increased difficulty listening to speech in noisy environments. In the current study, we examine the role of selective attention in SiN performance by comparing normal hearing listeners with those who have a cochlear implant (CI). CIs are an increasingly common approach for remediating severe to profound hearing loss and could potentially aid SiN performance by amplifying a target sound. In the current EEG study, 14 (n =14) patients with CIs and 20 (n = 20) normal hearing listeners completed a two-stream target detection task with a pre-trial (written) cue indicating which auditory stream (“Up” vs. “Down”) to attend to. On each trial, the word “Up” was presented five times, every .8 s, with a female voice, while “Down” was repeated four times, every 1 s, with a male voice. In normal controls, we observed clear signs of attentional modulation. To cued targets, there was greater cortical auditory evoked responses and cortical phase synchronization (inter-trial coherence). In CI users, however, there was inconsistent evidence for attentional modulation of cortical evoked responses. This suggests that poor auditory selective attention is one of limiting factors for CI users’ SiN difficulty.

96 Neural oscillations and nursery rhymes; A longitudinal EEG study into individual differences in infant language development

Adam Attaheri(1), Aine Ni Choisdealbha(1), Perrine Brusini(1), Sinead Rocha-Thomas(1), Sheila Flanagan(1), Natasha Mead(1), Panagiotis Boutris(1), Samuel Gibbon(1), Helen Scott(1), Henna Ahmed(1) and Usha Goswami(1)

(1) University of Cambridge

The synchronisation of cortical oscillations to temporal information in the speech signal may be central to language processing. Here we study the entrainment of low frequency neural oscillations (delta band, ~2Hz, and theta band, ~5 Hz) to both speech and non-speech inputs in infants. In spoken language, the production of stressed syllables occurs approximately twice a second across languages, and the modulation peak in infant directed speech is in the delta band. Accordingly, accurate entrainment to a 2 Hz ""beat"" may be crucial regarding individual differences in the acquisition of language.

We are conducting a longitudinal assessment of 113 infants from 2 months to 2.5 years of age, using EEG to measure oscillatory entrainment to different inputs (2Hz drum beat, 2Hz syllable repetition, nursery rhymes). We measure entrainment in 8 sessions across the first year of life (2-11 months) and follow language outcomes between 12 and 30 months, via phonological, morphological and vocabulary assessments.

We report preliminary findings from half our sample, showing that individual differences in the EEG responses to nursery rhymes at 4, 7 and 11 months predict language outcomes. We use a linear modelling technique (mTRF toolbox) for stimulus envelope reconstruction, and find correlations between reconstruction accuracy and language comprehension at 18 months. Secondly, we report phase-phase (PLV) and phase-amplitude coupling (PAC) in response to nursery rhymes from 4 months, with interesting changes longitudinally during the first year of life.

These results show the potential importance of individual differences in early neural entrainment in predicting later language outcomes."

97 Imaging the representation of sound location in the auditory cortex of awake marmoset

Chenggang Chen (1), Xindong Song (2), Yueqi Guo (3), Xiaoqin Wang (4)
(1) Johns Hopkins University
(2) Johns Hopkins University
(3) Johns Hopkins University
(4) Johns Hopkins University

Despite several decades of research, the nature of neural representation of sound location in auditory cortex remains unclear. Previous studies have failed to identify any maps or organization of spatial representation in mammalian auditory cortex. A prevailing hypothesis of cortical spatial processing is the distributed population coding, supported by the evidence that neurons responding broadly to sound locations on the contralateral hemifield. Recent electrophysiology studies in awake marmosets showed spatially highly selective cortical neurons and diverse spatial receptive fields across cortical surface. However, single or multi-unit electrophysiology method has limited power to evaluate both local and global organizations of cortical representation of sound locations. In the present study, we took the advantage of the flat brain of the marmoset, a highly vocal New World monkey, and used wide-field optical imaging methods to investigate the neural representations of sound location in auditory cortex in awake condition. The sound stimuli were Gaussian noises delivered in free-field on the horizontal plane from both contralateral and ipsilateral locations. Using wide-field calcium imaging method, we observed systematic changes in cortical response patterns as the spatial location varied along the azimuth axis. The pixels corresponding to the maximum responses to one of the tested sound locations formed clear clusters in the core region of the auditory cortex. These clusters were relatively stable across multiple sound levels. In addition, the pixels that showed strong calcium response to particular spatial stimuli also showed large hemodynamic changes as revealed by intrinsic imaging. These observations suggest that cortical neurons with similar spatial receptive fields may form local clusters in marmoset auditory cortex.

98 Multi-scale neural sensitivity to context

Tamar I Regev (1), Geffen Markusfeld (2), Israel Nelken(1,3), Leon Y Deouell (1,2)
(1) Edmond and Lily Safra Center for Brain Science
(2) Department of Psychology
(3) Department of Neurobiology

Everyday auditory stimuli, such as in music and speech, contain relevant information over multiple time and frequency scales simultaneously. We demonstrate sensitivity of ERP components to the distribution of auditory frequencies in unattended tone sequences. In three EEG experiments, 82 participants (21, 28 and 33 in Experiments 1, 2 and 3, respectively) were instructed to ignore tone sequences while viewing a silent film. The sequences were comprised of five equiprobable tones. The tones' frequencies were distributed across four octaves in Experiments 1 and 2, while in Experiment 3 this range varied between large, medium, and small (4, 2 or 1 octaves, respectively). We found that the amplitude of the N1 EEG component, peaking about 100 milliseconds after tone onset, was sensitive to a global feature - the interval between the current tone's frequency and the mean frequency of the tones in the sequence: The farther the tone's frequency from the mean, the larger the evoked N1 amplitude. In contrast, the P2 component, peaking about 200 milliseconds after tone onset, showed a temporally local sensitivity to the interval between the current and previous tones' frequencies, and a weaker sensitivity to the sequence mean frequency. These results were replicated across the 3 experiments. We propose a simple biophysical model of adapting neurons with wide frequency tuning curves and multiple adaptation time constants to explain these results. Further, the estimated width of tuning curves depended on the spread of frequencies in the sequence, for P2 but not for N1. Our results give electrophysiological evidence for pre-attentive simultaneous monitoring of context at multiple timescales in the human auditory cortex.

99 Neural activity in the auditory cortex during memory formation of auditory patterns

HiJee Kang (1), Ryszard Auksztulewicz (1), Hyunjung An (1), Mitchell Sutter (2), Jan Schnupp (1)
(1) City University of Hong Kong
(2) University of California, Davis

Learning and memory processes through repetitive exposure to target sounds are one of key factors for efficient auditory processing. Fast and robust memory formation of initially random, complex sounds as well as neural correlates of such memory in normal hearing humans have been previously reported (Agus et al., 2010; Andrillon et al., 2015; Luo et al., 2013). However, further in- depth neural recordings are required to identify neural mechanisms underlying memory formation. The present study aims at investigating the neural basis of learning and memory for initially random auditory patterns by recording neural activity in rodents. We examined seven female Wistar rats (8-11 weeks) using electrocorticography (ECoG) recording over the auditory cortex (AC) under anaesthesia. Random sparse tone clouds (cloud duration: 1 s; tone duration: 20 ms; 16 tones total) were used as stimuli. Tone clouds were either random for the whole duration (random tone clouds, T), or 0.25 sec. frozen random segment immediately repeated four times (repeated tone clouds, RT). While each stimulus type was generated afresh for 100 trials within one test block, one target RT (reference repeated tone clouds, RefRT) kept its characteristics and re-appeared for another 100 trials, presented in a randomised order. Five different RefRTs were generated for each test block, and two test blocks with the same RefRT were consecutively played. Greater neural responses for RefRT were observed compared to RT and T during sound presentation. To verify whether this difference is not simply due to unbalanced number of new patterns between RefRT and other stimulus types, we analysed the signal-to-noise ratio (SNR) of response amplitudes during the sound presentation relative to silence for each stimulus type and trial. Greater SNR for RefRT compared to RT and T started to emerge after about 10 trials. This effect remained robust until the end of the test block and continued from the first trial of the following test block containing the same RefRT. In line with previous human behaviour and neuroimaging studies, this finding indicates a fast formation of neural activity in the AC specific to re-occurring sound patterns. The results also establish an animal model of macroscopic neural correlates of memory formation and provide a useful basis for further micro- and mesoscopic neural recordings in individual neurons, impossible to achieve in humans, which will enable a deeper understanding of neural mechanisms of perceptual memory formation.

100 Characterizing the spatiotemporal pattern of neural activity and word representation during visual word recognition

Laura K Long (1,2), Minda Yang (1), Michael Sperling (3), Ashwini Sharan (3), Bradley Lega (5), Alexis Burks (5), Greg Worrell (6), Robert Gross (7), Barbara Jobst (8), Kathryn Davis (9), Kareem A Zaghloul (10), Sameer Sheth (1), Sandhitsu Das (9), Richard Gorniak (3), Paul Wanda (4), Michael Kahana (4), Joshua Jacobs (1), Nima Mesgarani (1,2)

(1) Columbia University
(2) Mortimer B Zuckerman Mind, Brain, & Behavior Institute
(3) Thomas Jefferson University Hospital
(4) University of Pennsylvania
(5) University of Texas Southwestern
(6) Mayo Clinic
(7) Emory School of Medicine
(8) Dartmouth Medical Center
(9) Hospital of the University of Pennsylvania
(10) National Institute of Neurological Disorders & Stroke

Visual word recognition (VWR) is the process of mapping the written form of a word to its underlying linguistic item. Characterization of healthy VWR neural mechanisms holds promise for improving treatment of reading deficits and deepening our understanding of literacy. While noninvasive neuroimaging studies have identified putative brain regions and event-related potentials involved in VWR, the spatiotemporal flow of information through the brain remains unclear. In this study, we analyzed high gamma neural activity of more than 13000 electrodes from more than 140 intracranial neurophysiology patients as they read visually-presented words. We find that over 3000 electrodes show a task-sensitive response. Latency analyses reveal that on average, occipital lobe electrodes respond fastest, followed by temporal lobe, with the slowest responses from frontal and parietal lobes. Middle occipital gyrus and fusiform gyrus are among the fastest regions on average. By clustering the responses of all task-sensitive electrodes, we identified a variety of response types including excitatory and inhibitory responses, onset and offset responses, and responses sustained for the duration of the word presentation. We observe that occipital lobe has the highest proportion of excitatory responses while frontal lobe has an almost even excitatory/suppressive balance. Furthermore, we investigated the neural representation of the stimuli's visual, phonemic, lexical, and semantic features. From each feature set, we predicted each electrode's response and investigated the properties of the best-predicted electrodes.Visually-predicted and phoneme-predicted electrode groups had mostly low latencies and excitatory peaks. Visually-predicted electrodes were spread between occipital and frontal lobes. Lexically- and semantically-predicted electrode groups included more suppressive responses, with linguistically-predicted electrodes distributed across frontal, temporal, and occipital lobes, and a plurality of semantically-predicted electrodes in frontal lobe. We further investigated the encoding of these electrode groups of the feature sets over time, showing that visual features peak quickly after word onset, followed by phonemic, linguistic, then semantic features. Together, these results provide a high-resolution look at the spatiotemporal pattern and representation of neural activity during visual word recognition in the human brain

101 Phonological feature and pitch classification with a branched convolutional neural network

Ian M. GRIFFITH (1), Shailee JAIN (2), Alex. G. HUTH (3,2), Liberty. S. HAMILTON (1,4)
(1) Dept. of Communication Science and Disorders, Univ. of Texas At Austin
(2) Dept. of Computer Science, Univ. of Texas At Austin
(3) Dept. of Neuroscience, Univ. of Texas At Austin
(4) Dept. of Neurology, Dell Medical School, Univ. of Texas at Austin

While processing natural speech, the human brain is able to take a complex acoustic signal and transform it into linguistically meaningful content. This includes encoding of simple acoustic features such as frequency or spectrotemporal modulation content, as well as phonological and prosodic representations. Previous research using invasive intracranial recordings has shown that distinct regions of the superior temporal gyrus encode prosodic and phonetic content (Tang et al. 2017). These regions are sensitive to intonational pitch (both absolute and relative) or phonological features, while being invariant to other stimulus features. However, it is not known how such invariance arises from auditory neural networks. To address this, we used a branched convolutional network trained on several hours of natural speech. Our network architecture consists of separate absolute pitch and phonological feature branches, each receiving input from shared earlier network layers. The network was optimized to simultaneously perform both absolute pitch and phonological feature classification, allowing earlier shared feature maps to inform individual task-specific outputs. Confusion matrices generated during model evaluation on a separate dataset indicate a high degree of accuracy and precision in both absolute pitch and phonological feature classification tasks. We next tested whether the representations learned by the network were able to predict brain responses. Using fMRI data collected from participants as they listened to the same natural speech stimuli, we fit encoding models that predict BOLD signals in each voxel using the activation weights from each layer of the convolutional neural network as stimulus features. Both pitch- and phonological feature-trained branches of the network strongly predicted activity in early auditory cortex in both the left and right hemispheres. We compare the spatial distributions of model performance to find regions of auditory cortex that differentially encode these intermediate to late layer representations. These results have implications for how invariance to complex attributes of speech and other natural sounds arise from earlier acoustic representations.

102 Deficits in central auditory processing in mouse models of Alzheimer's disease

Kelly A. Fogelson (1), Jennifer Lawlor (1), Ziyi Zhu (1,2), Kishore V. Kuchibhotla (1,2)
(1) Psychological and Brain Sciences, Johns Hopkins University, Baltimore, MD
(2) Department of Neuroscience, Johns Hopkins University, Baltimore, MD

Alzheimer's disease (AD) is a form of dementia that is characterized by the progressive loss of cognitive capacity, including the loss of executive functions and memory. There is growing evidence that hearing loss and dementia are tightly linked, with recent studies showing that hearing loss is independently associated with accelerated cognitive decline. However, the neural mechanisms linking hearing loss to AD-related pathologies and subsequent cognitive decline remain unknown.
We will test the hypothesis that amyloid pathology impacts feedforward sensory processing and short-term sensory memory formation in primary auditory cortex (A1). We performed in vivo two-photon calcium imaging in awake, head-fixed APPswe/PS1dE9 (APP/PS1) mice to investigate how AD pathology impacts central auditory processing. APP/PS1 mice express chimeric mouse/human amyloid precursor protein (APP) and mutant presinilin-1 (PS1). These transgenes target neurons of the central nervous system, and lead to the rapid accumulation of soluble amyloid beta and subsequent plaque deposition in cortical and hippocampal areas.
Our study uses the fine-scale tonotopic arrangement of excitatory neurons in A1 as an assay for feedforward sensory integration. With two-photon calcium imaging, we have the spatial and temporal resolution to monitor the activity of hundreds of neurons simultaneously with single-cell resolution. Preliminary data collected from 11 mice (7 APP+, 4 WT) suggests clear differences in the processing of feedforward sensory information, namely differences in the tonotopic arrangement of neurons in A1 between WT and APP/PS1 mice.
In contrast to tonotopy which is largely inherited from sub-cortical structures, the auditory cortex plays an active role in the formation of sensory memories, including in stimulus-specific adaptation (SSA). SSA is the reduction in firing rate to a repeated stimulus which does not generalize to an alternative rare and infrequent stimulus. We aim to characterize SSA to determine how AD pathology impacts the formation of sensory memories.
Future work will investigate how AD pathology affects sensorimotor learning. Learning rates will be monitored in APP/PS1 mice trained on a go/no-go stimulus recognition task. To probe the neural computations that are critical for the selection of auditory cues during behavior, excitatory networks in A1 will be monitored using two-photon calcium imaging while animals perform the task. This study hopes to elucidate neural mechanisms of how amyloid beta pathology impacts central auditory processing, and thus, mechanistically link hearing loss, Alzheimer's-related pathologies and cognitive impairments."

103 Rapid pupil dilations accompany unexpected self-generated sounds in mice

Hoda Ansari (1), WenXi Zhou (1), Megha Kori (1), David M. Schneider (1)
(1) New York University

The sounds generated by our actions are often predictable. For example, shutting a car door produces a recognizable acoustic "thump" that is linked in time to one's forelimb movements. Humans and other animals can learn the associations between particular actions and their expected acoustic outcomes and can use these expectations to detect violations. In humans, songbirds, marmosets, and mice, neural activity at the level of the auditory cortex reflects expectation violations during a variety of sound-generating behaviors. And in humans, surprising sounds are associated with changes in pupil diameter. However, to our knowledge it remains unknown whether expectation violations are reflected in the pupil of mice.

To address this, we trained mice to perform a simple behavior that produces a predictable self-generated sound. Head-restrained mice pulled a lever ~6 mm using their right forelimb, resulting in a small liquid reward that was delivered after they returned the lever to the home position. During an initial phase when mice were learning the task, successfully moving the lever produced a reward but no sound. After 2 days of stable lever movements, we introduced without warning a self-generated tone that was predictable in frequency (e.g. it was always 8Khz) and time (e.g. it was always played immediately after mice pulled the lever past the 6 mm threshold). After 2 days experiencing a stable and predictable self-generated sound, we introduced infrequent oddball tones that deviated from the expected frequency. As mice operated the lever, we simultaneously monitored their forelimb movements and the diameter of their pupil.

Lever movements were accompanied by pupil dilations that began hundreds of milliseconds prior to moving and lasted hundreds of milliseconds after the movement was complete. During the first few lever movements that produced self-generated sounds, pupil dilations were larger than observed during silent movements. This tone-related dilation often subsided over several tens of movements, suggesting that the enhanced dilation reflected surprise rather than sensation, per se. Consistent with this interpretation, lever movements accompanied by tones of an unexpected frequency produced greater pupil dilations than did lever movements accompanied by expected tones of the same intensity.

Together, these experiments suggest that deviations from expectation are reflected in rapid changes in pupil diameter in mice. Moreover, they suggest a simple and translatable assay of expectation violation that is consistent with electrophysiological recordings in the auditory cortex of many species, including humans. Ongoing experiments are exploring whether pupil diameter reflects expectation violations in other acoustic dimensions (e.g. timing, intensity) and other forms of predictability.

104 High angular resolution diffusion-weighted MRI exploration of the homotopic and heterotopic connectivity of human auditory cortex.

Iman A. Nassar (2), Omar A. Ibrahim (1), Issam Tafech (1), Jaakko Kauramäki (3), Marc Schönwiesner (3) & Julien Besle (1)
(1) Department of Psychology, American University of Beirut, Beirut, Lebanon
(2) Neuroscience Research Center, Lebanese University, Beirut, Lebanon
(3) International Laboratory for Brain Music and Sound Research (BRAMS), Université de Montréal, Québec, Canada

Introduction: Recent fMRI tonotopic mapping of the human auditory cortex suggests that its functional organization may substantially differ from that of non-human primates [1]. In this study, we further compare the human functional organization to the primate model by studying the pattern of connections between functionally distinct areas of human auditory cortex and their relationship to tonotopic organization using MRI.
In non-human primates, the medial geniculate nucleus mostly projects to auditory cortical core areas; core areas mostly project ipsilaterally to nearby core and belt areas, as well as to their contralaterally corresponding core area; finally, intrinsic connections in A1, as well as extrinsic connections between both ipsilateral and contralateral core areas are mostly between tonotopically-matched locations (extrinsic homotopic). There have been very few studies of the thalamo-cortical and cortico-cortical connections in human auditory cortex, and to date only one included functional tonotopic measurements. Although one previous diffusion-weighted MRI study in humans reported a hierarchical connection pattern between putative core, belt and parabelt areas [2], similar to the one described above in primates, another study found a larger number of heterotopic than homotopic tracks [3], which seems to contradict the primate findings.
Here, we combined fMRI-based tonotopic mapping and diffusion-weighted-MRI-based probabilistic tractography and estimated the number and density of tracks connecting auditory cortical regions tuned to the same or different frequencies (homotopic or heterotopic connections), located in the same or different auditory cortical fields (intrinsic or extrinsic connections) and in the same or different hemispheres (ipsilateral or contralateral connections). In addition, we attempted to track the auditory radiation connecting the MGB to the auditory core.
Methods: We acquired structural, functional and diffusion-weighted MRI data from the same 16 participants as part of two separate studies at Université de Montréal and the American University of Beirut. Structural scans (T1-weighted MPRAGE, resolution 0.7 or 1 mm) were used to reconstruct the cortical surfaces of each participant. Functional tonotopic scans (sparse GE-EPI, TR= 8s, resolution 1.5mm in-plane) were used to estimate responses to pure tones at 8 centre frequencies between 0.2 and 8 kHz and derive each voxel's preferred frequency. We used automatic detection of tonotopic gradient reversals to delineate regions of interests (ROIs) corresponding to tonotopically-organized areas on the cortical surface, in particular mirror-reversed tonotopic gradients located on Heschl's gyrus that may correspond to core areas. We further subdivided these ROIs divided into isotopic regions at different frequencies.
Diffusion-weighted scans (SE-EPI, resolution 2 mm) were acquired at 3 or 4 b values (9 or 7 × b = 0; 7 or 0 directions at b = 300, 31 directions at b = 1000 and 63 directions at b = 2000 s/mm2). We estimated fibre orientation distributions using multi-tissue, multi-shell

constrained spherical deconvolution. The location of the MGB was identified from super-resolution track-density maps derived from a whole-head tractography. Number and density of tracks were then estimated for all reciprocal connections between all MGB and functionally-defined ROIs using a probabilistic tracking algorithm.

Preliminary results (limited to ipsilateral cortico-cortical connections between frequency-specific regions of the two mirror-reversed tonotopic gradients on Heschl's gyrus): extrinsic homotopic connections between high-frequency regions had less tracks than extrinsic heterotopic connections (confirming previous diffusion-functional results [3] and apparently contradicting the animal literature), which in turn had less tracks than extrinsic homotopic connections between low-frequencies regions or intrinsic heterotopic connections. The full pattern of connections however could be explained by an effect of the distance between ROIs on the number of tracks found. Track density did not significantly differ between any connections.

Preliminary conclusion: The effect of distance between subcortical and cortical connection targets must be properly accounted for before diffusion-weighted MRI can be meaningfully compared to connectivity results obtained invasively from animal models.

1. Besle, J., et al., Is human auditory cortex organization compatible with the monkey model? Contrary evidence from ultra-high-field functional and structural MRI. Cerebral cortex, 2019. 29(1): p. 410-428.

2. Cammoun, L., et al., Intrahemispheric cortico-cortical connections of the human auditory cortex. Brain Struct Funct, 2015. 220(6): p. 3537-53.

3. Upadhyay, J., et al., Function and connectivity in human primary auditory cortex: a combined fMRI and DTI study at 3 Tesla. Cereb Cortex, 2007. 17(10): p. 2420-32.

105 Reliable envelope coding from unreliable single neurons

Kristina Penikis (1), Dan Sanes (1)
(1) New York University

While natural acoustic signals, including speech and music, often contain rhythmic elements, the amplitude modulations (AM) composing them are temporally irregular. However, our understanding of AM coding is largely based on periodic stimuli, with responses typically measured from activity averaged over many iterations of each period. Since auditory response properties are sensitive to stimulus history and vary from trial-to-trial, we first asked how temporal regularity impacts coding by individual neurons. Single unit recordings were obtained wirelessly from gerbil auditory cortex (NeuroNexus 16 and 64 channel arrays) as gerbils performed an aversive Go-Nogo detection task in which all modulated stimuli were safe (signaling the availability of a water reward), while unmodulated noise served as the warn signal that predicted a brief electrical shock. Modulated stimuli were either periodically sinusoidally modulated at rates of 2-32 Hz, or aperiodically modulated (i.e., quasi-random sequences of individual periods drawn from the same set of rates). In addition, we characterized responses to vocoded speech stimuli. We found that responses of individual neurons to a given AM period could be modulated by stimulus history, but high trial-to-trial variability led to low discriminability across stimulus history contexts. High response variability raises the question of how neurons can provide a robust representation of the envelope of a complex signal in real time. Our recordings suggest that cortical responses tile the complex envelope. Therefore, our current analyses focus on assessment of how larger pools of units enhance the representation of irregular AM sequences, including vocoded speech.

106 Speech encoding from simultaneous ECoG recordings of human temporal plane and lateral temporal cortex

Liberty S. Hamilton (1,2), Yulia Oganian (1), Edward F. Chang (1)
(1) University of California, San Francisco
(*2) University of Texas at Austin*

Speech processing involves the transformation of information from acoustic to phonetic and higher-order linguistic categories. Intracranial recordings have contributed significantly to understanding this transformation, however limitations in surgical exposure have precluded simultaneous high-density sampling from core and surrounding auditory cortices. Our previous work has demonstrated encoding for acoustic-phonetic features, spectrotemporal modulation, and intonational pitch tuning in superior temporal gyrus (STG), as well as a posterior region of the STG that is specialized for detecting acoustic amplitude onsets, but how this relates to processing in core auditory cortex is less well understood. Here, we present a functional characterization of the entire human auditory cortex, including the core and surrounding belt/parabelt areas. We overcame previous limitations by using direct recordings from the surface of temporal plane after surgical microdissection of the deep recesses of the Sylvian fissure when indicated for clinical purposes (peri-Sylvian epilepsy or insular tumors). We obtained simultaneous high-density recordings from patients with high-density electrode grids over the temporal plane (including Heschl's gyrus, planum temporale, and planum polare) and also over the lateral superior temporal gyrus in the left hemisphere. We then recorded neural responses while participants listened to natural speech sentences and non-speech pure tone stimuli. We fit models combining acoustic and linguistic stimulus representations to predict neural responses. We also compared latencies across different auditory fields and functional areas. Speech activated much of the temporal plane and STG, including belt and core areas. Heschl's gyrus and planum temporale exhibited strong, narrow-bandwidth tone responses, and strong responses to speech, while phonetic feature representations dominated in mid-STG. This study provides a comprehensive characterization of feature encoding for speech across the human auditory cortex at high spatiotemporal resolution.

107 Behavioural and neural measures of auditory regularity detection in ferrets

Katarina C. Poole (1), Eleanor J. Jones (1), Maria Chait(1), Jennifer K. Bizley(1)
(1) University College London

To understand complex acoustic environments humans and animals are able to segregate and maintain auditory streams during auditory scene analysis (ASA). To perform efficient scene analysis, the brain is able to utilise stimulus statistics, ongoing context and temporal structure to extract regularities and predict future acoustic events. As a result, acoustic stimuli that transition from randomly occurring to regularly repeating pure tone sequences have recently been employed as an objective measure to investigate ASA (Barascud et al., 2016).

We trained ferrets (n=3) on a go/no-go task where the animals are required to detect the transition from a random sequence of tones (50ms duration) to a regularly repeating sequence (repeat length 3 tones, duration 150ms), and simultaneously in a visual task where a continuously lit LED transitions to a flashing LED (flash interval 150ms). During pilot experiments, all animals were able to perform significantly above chance (Monte-Carlo simulation) in each modality (Auditory: $p < 0.001$, d' range across animals = 1.02 to 1.70; Visual: $p < 0.001$, d' range across animals = 1.7 to 2.03). To test increasingly complex auditory patterns, repeat lengths were then varied in further experiments from 3 to 5 and 7 tones with most animals performing above chance in all pattern lengths with a decrease in performance with increasing pattern complexity (e.g. respective mean d' across animals (n = 2): 1.44, 1.04, 0.85, $p < 0.01$).

With these data paving the way for investigating regularity detection, we aim to identify the neural correlates of this auditory process by recording local field potentials and spiking activity in the auditory cortex and hippocampus of trained animals engaged in this behavioural task, with comparison to neural activity in passive naïve animals.

References:

Barascud, N., Pearce, M.T., Griffiths, T.D., Friston, K.J., and Chait, M. (2016). Brain responses in humans reveal ideal observer-like sensitivity to complex acoustic patterns. PNAS 113, E616–E625.

108 Multi and single unit neuronal activity in human Heschl's gyrus during speech perception and production

Araceli Ramirez-Cardenas (1), Roozbeh Behroozmand (2), Christopher K. Kovach (1), Phillip E. Gander (1), Ryan Kelley (1), Kirill V. Nourski(1), Hiroyuki Oya (1), Hiroto Kawasaki (1), Mathew A. Howard III (1), Jeremy D. Greenlee (1);

(1) University of Iowa (2) University of South Carolina

Suppression of responses to self-generated sounds within auditory cortex has been extensively investigated in human neuroimaging and animal neurophysiology studies. Vocalization suppresses activity in auditory cortex relative to activation elicited by speech playback. This modulation of auditory neural responses is deemed essential for monitoring speech production. Auditory suppression is thought to be subserved by a circuit that compares forward predictions with actual sensory feedback. To study the neural networks involved in speech control, we delivered an online perturbation in the auditory feedback while subjects vocalized. Auditory feedback was shifted in either the frequency or time domain for a variable short period in pseudorandomized trials. Voice was recorded and subsequently played back to the subjects for comparisons between auditory and motor activity. We recorded LFPs, multiunit and single-unit activity from Heschl's gyrus (HG) in 17 neurosurgical patients undergoing epilepsy surgery evaluation.

We found that neural activity was differentially modulated by the start of auditory feedback in posteromedial and anterolateral HG. Moreover, multiple single neurons showed differential responses to auditory feedback during listening vs. speaking conditions. Consistent with animal studies, some of these neurons exhibited an attenuated response to auditory feedback during vocalization. This suppression, relative to baseline activity started at least 100 ms before the onset of auditory feedback and peaked shortly after. This finding is interpreted as a potential neuronal correlate of speaking-induced suppression of human auditory cortex. Moreover, we found multiple neurons in which excitatory neuronal responses were elicited during both listening and speaking conditions. We further analyzed the frequency tuning properties of these two neuronal subpopulations in the auditory cortex and investigated their role in error detection when auditory-feedback was perturbed. Based on previous reports from marmoset studies, we hypothesize that neurons exhibiting motor-induced suppression would play a prominent role in the detection of auditory-feedback perturbations. Moreover, we compared the behavioral contribution of these neuronal subpopulations in the trial-by-trial motor responses to perturbed auditory feedback. Finally, we analyzed the extent to which single and multiunit spike responses in the human HG could predict the LFP responses extracted from the same and adjacent recording sites.

109 Neural encoding and decoding of auditory cortex during perceptual decision making

Akihiro Funamizu (1), Fred Marbach (1), Anthony M. Zador (1)
(1) Cold Spring Harbor Laboratory

Neurons in auditory cortex encode auditory stimuli, but the precise encoding can depend strongly on task-relevant variables such as stimulus or reward expectation. This raises the question: If the cortical representation of the stimulus varies with task-relevant variables, how can areas downstream of auditory cortex decode these representations? One possibility is that decoding in downstream areas also depends on these task-relevant variables. To address this question, we developed a two-alternative choice auditory task for head-fixed mice in which we varied either reward expectation (by varying the amount of reward, in blocks) or stimulus expectation (by varying the probability of different stimuli). We then used calcium imaging to record populations of neurons in auditory cortex while mice performed the task. We found that varying either reward or stimulus expectation changed neural representations (i.e. stimulus encoding), sometimes dramatically. However, the optimal decoder was remarkably invariant to different encodings induced by different expectations. Our results suggest that stimuli encoded by auditory cortex can be reliably read out by downstream areas, even when the encoding is modulated by task-relevant contingencies.

110 Neuromodulatory- and prefrontal- sensory cortical interactions underlying motivated shifts in attentional effort

Zakir H. Mridha, Jan Willem De Gee, Yanchen Shi, Hannah Ramsaywak, Anton Banta, Wenhao Zhang, Matthew J. McGinley (1)

(1) Baylor College of Medicine, Department of Neurscience and Duncan Neurological Research Institute

Humans and other animals constantly adapt their allocation of cognitive resources to changes in the environment. In sensory domains, the brain is capable of enhancing the processing of difficult-to-perceive stimuli when they are important (Kahneman, 1973). In the context of perceptual decision-making, this is referred to as attentional effort (Sarter et al., 2006), and in the auditory field it is a major component of 'listening effort.' In contrast to the extensive study of e.g. the selective aspect of attention (Desimone and Duncan, 1995), the neural circuit mechanisms of attentional effort are poorly understood. Key candidate mechanisms are direct neuromodulation of sensory cortex (Aston-Jones & Cohen, 2005), and bi-directional interactions of sensory and frontal cortical regions (Miller & Cohen, 2001). Here, we seek to determine the neural circuit basis of attentional effort. We developed an attentional effort (AE) task for head-fixed mice. In the AE task, mice lick for sugar-water reward to report detection of the unpredictable emergence of temporal coherence in an ongoing tone cloud, analogous to coherent motion in common visual attention tasks. Perceptual difficulty is parametrically and unpredictably varied, trial-by-trail, through partial degradation of the coherence. To manipulate attentional effort, we alternate between a large and small reward volume in blocks of 60 trials. Thus, mice are motivated to expend more attentional effort in blocks with large rewards.

Increased attentional effort in high-reward blocks manifested as increased sensitivity (d' from SDT) to detect coherence in noise (2-way rmANOVA $F_{1,21} = 38.5$; $p < 0.0001$; N=22 mice), particularly for weak-coherence targets (interaction $F_{2,42} = 11.7$; $p < 0.0001$). Mice exhibited >5 effort shifts within each session, tightly time-locked to block changes. In addition, contrary to the trivial prediction that high reward increases global neuromodulator levels (arousal), mice decreased their arousal in high reward blocks, apparent in baseline pupil size ($p = 0.002$). Thus global neuromodulation doesn’t account for attentional effort. Finally, feedback pupil responses exhibited multiple signals reflecting flexible AE regulation, including: correctness, reward context, and prediction errors. In ongoing 2-photon GCaMP imaging, we are determining the roles of frontal-sensory and neuromodulatory signals in mediating these shifts in overt behavior.

References: Kahneman (1973), Prentice-Hall. Aston-Jones & Cohen (2005), Annu. Rev. Neurosci., 28, 403-450. Desimone & Duncan (1995), Annu. Rev. Neurosci, 18(1), 193-222. Sarter, Gehring, & Kozak (2006), Brain Res. Rev., 51(2), 145-160. Miller & Cohen (2001), Annu. Rev. Neurosci., 24(1), 167-202.

111 Spectral cues are necessary for encoding the azimuthal map of auditory space in the mouse superior colliculus

Shinya Ito (1), Yufei Si (1), David A. Feldheim (1), Alan M. Litke (1)
(1) University of California, Santa Cruz

Sound localization plays a critical role in animal survival. To compute the incident sound direction, the animal can use three cues: interaural timing differences (ITDs), interaural level differences (ILDs) and the direction-dependent spectral filtering of the sound by the head and pinnae (spectral cues). ITDs and ILDs have been considered to be the two primary cues used for sound localization in the horizontal plane. On the other hand, spectral cues were hypothesized to be used for resolving directions that the ITDs and ILDs cannot distinguish, namely, for resolving the front–back ambiguity and for determining the sound source elevation. However, little is known about how spectral cues contribute to the neural encoding of the map of azimuthal auditory space. To fill this knowledge gap, we investigated the auditory space encoding in the mouse superior colliculus, using virtual auditory space stimuli. We show that the mouse SC contains neurons with receptive fields (RFs) that form a topographic map of azimuthal auditory space. By eliminating each sound localization cue from the stimuli, we found that nasal RFs require spectral cues and temporal RFs require ILDs. Therefore, the lack of either cue results in the disruption of the azimuthal topographic map. Based on these findings, we developed a mathematical model that recapitulates our data. These results demonstrate an unexpected role of spectral cues for the azimuthal auditory map, lending new insights into how mammals perform sound localization and indicate that the mouse is a useful model to study the mechanisms of auditory processing.

112 Cortical dynamics of word-in-noise recognition in cochlear implant users

Subong Kim (1), Jason Geller (2,3), Ann Holmes (2,3), Bob McMurray (1,2,3), Inyong Choi (1,2)
(1) Communication Sciences and Disorders, University of Iowa
(2) Department of Otolaryngology-Head and Neck Surgery, University of Iowa Hospitals and Clinics
(3) Department of Psychology and Brain Sciences, University of Iowa

Spoken language processing is an incremental process that unfolds over time. As a result, there is much ambiguity early on in language processing. This process is made more difficult in noisy listening environments. A primary clinical concern in cochlear implantation (CI) patients is being able to recognize speech-in-noise (SiN). Given this, characterizing neural correlates of individual differences in CI users' SiN understanding is critical. This study investigated neural factors that predict CI users' word-in-noise understanding accuracy, focusing on temporal characteristics of cortical activities. More specifically, we explored the relationship between the time course of lexical access (measured by eye fixation proportions in a visual world paradigm) and the evoked response at cortical regions-of-interest (measured by high-density electroencephalography (EEG)) in a SiN task. Our correlational analysis between the EEG and eye-tracking (i.e., fixation proportion) measures found that the strength of the auditory cortex response predicts the temporal dynamics of lexical competition. Both the EEG and eye tracker measures predicted behavioral performance in the word-in-noise test. These results suggest that temporal characteristics of cortical responses reflect the speed of lexical access, while such factors form critical neural correlates of individual differences in CI users' SiN understanding.

113 The Cognitive Computations of Metacognitive Sensitivity in Absolute Pitch Individuals

Tamara Tang (1), Megan A.K. Peters (1,2,3)
(1) Department of Bioengineering, University of California, Riverside
(2) Interdepartmental Graduate Program in Neuroscience, University of California, Riverside
(3) Department of Psychology, University of California, Riverside

It is known that music affects behavior and cognitive processing in humans. Specifically, it has been suggested that neural processes differ as a function of musical aptitude, and especially between individuals possessing absolute pitch (AP; the ability to precisely identify and name music tones in isolation) versus those who do not. While prior studies confirm the engagement of higher order cognitive processes during music processing, as well as highlight the specific brain areas involved (e.g. A1 and PFC), previous work has failed to precisely characterize the unique roles played by these regions -- as well as interactions among regions -- in driving or explaining musical expertise. This study explores the role of metacognitive sensitivity with regards to musical ability and auditory perceptual processing via a novel 2IFC (2-interval forced-choice) auditory pitch discrimination plus confidence-judgment task. We used signal detection theoretical metrics to quantify Type 1 and Type 2 (metacognitive) sensitivity of absolute pitch discrimination as a function of participants' musical training. Preliminary analyses suggest that metacognitive sensitivity is higher for subjects with musical training, validating our paradigm. Ongoing data collection pairs our novel task with 64-channel EEG recording and decoding analyses to reveal the computational and neural differences in pitch discrimination and metacognitive evaluation as a function of musical ability.

114 Effects of stochastically varying modulation frequency on the detection of amplitude-modulated noise

*Kevin N. O'Connor, Daniel. R. Johnson, Jeffrey. S. Johnson, Mitchell. L. Sutter
University of California, Davis

Amplitude modulated (AM) noise has been a useful tool for investigating temporal processing in auditory systems because no confounding spectral information is present. The vast bulk of research has been performed using sine-AM (SAM), which allows determination of AM sensitivity as a function of modulation frequency. Analysis of neural responses to SAM noise has produced two primary coding models, one based on spike rate and the other on the temporal pattern of spikes (Joris et. al. 2004), which for SAM, is roughly phase-locked to the oscillations in the signal.

One problem for this temporal coding scheme is the limitation in neurons' ability to follow fast oscillations as the auditory system is ascended. For this reason, it has been proposed that, for auditory cortex (AC), a rate code is used for high AM frequencies, while temporal coding occurs at lower frequencies (< ~60 Hz) where synchronous responding is prevalent (Wang 2008), though this is not a clear-cut distinction (Yin et. al. 2011; Johnson et. al. 2012). In macaque AC firing rate is more closely linked to behavioral AM detection than synchronicity, implying a greater role for firing rate in perception and decision making (Niwa et.al. 2012; 2013). To test for the role of synchronous following in encoding AM, we introduced stimuli whose modulation frequency varied stochastically about a center frequency (CMF) and across several modulation frequency ranges or bandwidths (MBWs). A simple phase-locking code should degrade as the variation about the CMF increases.
The ability of 3 listeners (3 adult males) to detect modulation in these stochastically modulated AM (400-ms) noise stimuli, as a function of modulation level, was tested. Modulation detection was tested at 2 CMFs (20 and 250 Hz) and at 3 MBWs (1, 2 and 4 octaves), and also for SAM noise at the CMFs. If synchronous phase-locked responding is important for detecting AM noise, detection should worsen with increasing MBW, and to a much greater degree for the 20 than 250 Hz CMF stimuli. We did find poorer detection with increasing MBW at both CMFs. Though there was no interaction between CMF and MBW, detection at 2 and 4 octave MBWs was notably worse for 20 Hz CMF stimuli. The results indicate that, although synchronous oscillatory neural activity may be a useful cortical temporal code at low frequencies, it is not essential.

115 Species differences in the cortical analysis of auditory time windows in primates

Pradeep Dheerendra (1), Simon Baumann (2), Olivier Joly (3), Fabien Balezeau (1), A lexander Thiele (1), Timothy D Griffiths (1)
(1) Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK
(2) Department of Experimental Psychology, Oxford University, UK
(3) Brainomix, Oxford, UK

We examined the brain basis for the processing of auditory time windows in stimuli with similar spectro-temporal complexity to human speech or macaque vocalisations. We created a synthetic stimulus by manipulating spectral flux, a timbral dimension, to systematically vary the time window duration required to analyse it. We conducted functional magnetic resonance imaging in awake macaques using this stimuli to test how the anatomy of their response patterns of time window processing compares to humans. Window of temporal integration was characterised in terms of the Pearson correlation (r) between amplitude spectra of adjacent timeframes [PMID 19052218] or in terms of time window within which any two frames show a minimum level of correlation thus shorter windows have lower r while longer windows have higher r. Individual core and belt areas were defined on 3 animals using tonotopic mapping and myelin mapping [PMID 25100930]. Sparse EPI images were acquired on a 4.7T vertical scanner whilst they carried out visual fixation. A general linear model analysis [SPM12] allowed single-subject inference to determine the relationship between BOLD and r in individual core and belt areas.

Despite a similar overall pattern of changing preference, from shorter time windows in postero-medial areas to longer time windows in antero-lateral areas, monkeys exhibited a reduced sensitivity to longer time windows as compared to humans [PMID 19052218]. This difference in sensitivity is in line with recent behavioural results and might be explained by a specialization of the human brain for speech processing which requires sensitivity to longer time windows. We highlight specifically human response patterns that suggest an adaptation of a general primate brain mechanism, possibly an outcome of divergent evolution alongside the development of speech.

116 Neural activity in mouse auditory cortex is influenced by context, behavior, and expectation

Nicholas J. Audette (1), David M. Schneider(1)
(1) New York University Center for Neural Science

Hearing is not simply about detecting sounds. To benefit from hearing, animals must perceive and respond to sounds in a way that is sensitive to behavioral context by integrating acoustic input with variables including environmental features, prior associations, and ongoing movement plans. Recent experiments have shown that movement, reward-relevance, and predictability can independently affect neuronal activity at the earliest stage of cortical processing. However, it remains unclear how these contextual variables interact with one another to influence sensory responses at the single neuron and population levels in the primary auditory cortex. To investigate this question, we developed a simple lever-press behavioral paradigm in which mice learn to make highly-stereotyped, reward-driven forelimb movements accompanied by auditory feedback. The relationships among movement, sound, and reward can be experimentally controlled to produce a variety of contexts and associations. Trained mice altered their behavior in response to tones that were omitted or presented at unexpected times, indicating that they learned the expected relationship between movement and sound. We then used dense multi-unit array recordings in performing mice to measure neural population activity in response to sensory stimuli with varying contextual properties. We find that average sound-evoked neural responses in primary auditory cortex are suppressed during self-generated movements compared to passive listening. Movement-based suppression was strongest for predictable tones while tones that deviated from an expected frequency evoked relatively larger neural responses. Surprisingly, strong neural suppression was present even when predictable tones were tightly linked with rewarded outcomes. Despite this population-level suppression, single-neuron analysis revealed that a subset of neurons was preferentially activated by expected tones, raising the possibility that predictability might sparsen - rather than dampen - neural responses to expected sounds. This closed-loop, lever-based behavior provides an experimental platform for studying how internal and external variables augment auditory processing, behavior, and perception.

117 Dynamics of primate inferior colliculus neurons during the localization of simultaneous sounds

Shawn M. Willett (1), Surya T. Tokdar (1), Jennifer M. Groh (1)
(1) Duke University

It is unclear how neurons and populations of neurons encode more than one stimulus. Canonically, a possible solution is to have sufficiently selective neurons so stimuli representations could be encoded by specific neural subpopulations. However, this proposed solution ignores the multi-selectivity of many neural populations, the surprisingly broad tuning of neurons, and the complex content of natural stimuli. For example, neurons in the monkey inferior colliculus encode sound location by monotonically increasing their firing rate with sound eccentricity, while they encode sound frequency with circumscribed, but broad, receptive fields. Recent work (Caruso et. al., Nature Communications, 2018) proposed an alternative to the selective subpopulation hypothesis and showed that some inferior colliculus neurons alternate between firing rates corresponding to two simultaneously presented sounds within single trials. However, this study only presented sounds of similar frequencies. It remains unclear if these dynamics exist when sounds of dissimilar frequencies are presented, where neural tuning for frequency may potentially carry a larger coding burden. The current study presented simultaneous sounds with variable separation of frequency to investigate the impact of frequency selectivity on the dynamics of single trials neural responses.

To determine the response functions of IC neurons, spiking activity from isolated, sound responsive, neurons were recorded while two rhesus macaques (Macaca mulatta) performed a dual sound localization task. The task required monkeys to make either a single saccade to the location of one sound or a sequence of saccades to the location of each simultaneously presented sound. Traditional time and trial pooled analyses found many of the neurons average their responses in the presence of two sounds. Upon closer inspection by an analysis using spike count distributions from single trials (whole trial, i.e. 1 bin) revealed some neurons alternate across trials. That is on some trials neurons responded to one sound and on other trials they responded to the other sound. Analyses at finer time scales in neurons that exhibited intermediate whole trial spike counts but did not show such fluctuations at the single trial level are currently pending

118 Changes in saccade-related eardrum oscillations after surgical denervation of the stapedius muscle

Stephanie Schlebusch (1), Matthew Cooper (1), David Kaylie (1), David L.K. Murphy (1), Cynthia King (1), Christopher Shera (2), Jennifer M. Groh (1)
(1) Duke University
(2) University of Southern California

The connection between the visual and auditory systems plays an important, integrative role in perceiving surrounding stimuli correctly. We have recently reported an oscillation of the eardrum time-locked with the onset of a saccade and in the absence of incoming sound that suggests this connection may begin as early as the auditory periphery. These eye movement-related eardrum oscillations (EMREOs) covary in phase and amplitude with the direction and magnitude of a synchronous saccade (Gruters, Murphy et al. PNAS 2018). However, the acting anatomical features and their joint contributions to this eardrum oscillation- possibly including the stapedius, tensor tympani, and outer hair cells - are still unknown. We first sought to determine the interactions between the stapedius muscle and the eardrum during saccade activity, an important initial step towards understanding both the mechanisms within the middle and inner ear that cause the EMREO and the function of the EMREO.

We recorded EMREOs in one rhesus monkey during a spontaneous saccade task before and after denervating and transsecting the stapedius muscle of one ear. The monkey was head-restrained in a dark room, and eye movements were tracked with a video eye tracker (1000 Hz sampling rate) while eardrum oscillations were recorded using microphones placed in the ear canals of both ears. We report pre-surgery that we can see a well-characterized, highly reproducible EMREO in both the left and right ear, and that the horizontal component of a saccade has significant input to an accompanying EMREO, as expected from previous work. We then performed surgical transsections of the facial nerve and stapedius muscle on the right side, thus completely denervating the stapedius as well as disconnecting it from the stapes bone of the middle ear. We retested the monkey during and after a four-month recovery period with the same pre-surgery recording methods. After surgical intervention of the stapedius muscle, characteristic EMREOs are not immediately apparent in the operated ear and regression analyses show that the input of the horizontal component of a saccade to an accompanying EMREO is significantly diminished (by about 30%), but not absent. The control ear maintains its pre-surgery, highly reproducible EMREO. Trial-wise analysis in the frequency domain suggests post-surgery changes in the frequency of oscillations of the eardrum in the operated ear and/or phase synchronization with respect to eye movement. Together, these findings suggest that there may be multiple contributors to the EMREO in a complex mechanism within the ear, and that the stapedius muscle is one of these contributors.

119 Two-photon calcium imaging of auditory processing in the echolocating bat

Melville Wohlgemuth (1,2), Jennifer Lawlor (1), Cynthia Moss (1), Kishore Kuchibhotla (1)
(1) Johns Hopkins University
(2) University of Arizona

As humans and animals operate in the natural world, they receive, process, and react to a wide variety of complex stimuli. To investigate how the brain sorts and differentially responds to environmental stimuli, we exploit an animal model long-studied for its active sensing in the natural world: the echolocating bat. The echolocating bat produces sonar vocalizations and listens to returning echoes to determine the identity and location of objects in the environment. The bat also modifies its vocalizations to extract different features of its acoustic scene, with specific adaptations in response to an object's distance, motion, or the presence of background clutter. The spectro-temporal changes in vocal parameters correspond to specific stimulus configurations in the bat's auditory scene and provide explicit information about the signals used to guide orienting behaviors. Central to sensorimotor integration is the midbrain superior colliculus (SC). The SC is a laminated structure, with dorsal layers primarily responsive to the location of objects in egocentric space, and ventral layers involved in generating orienting behaviors to environmental stimuli. In the bat SC, neurons in dorsal layers are selective to spectro-temporal features of sonar sounds and neurons in more ventral layers respond to a wider range of acoustic stimuli. We hypothesize that laminar differences in SC stimulus response selectivity are driven by network interactions of neighboring neurons. Traditional multi-channel electrophysiology techniques can only partially assay network level activity, and as such, we are establishing methods of two-photon calcium imaging in the echolocating big brown bat, Eptesicus fuscus, to assay population-level activity. We first tested several different adeno-associated virus (AAV) serotypes, as well as the efficacy of a variety of cell-specific promotors. Optimized AAV techniques to drive the expression of GCaMP6f are now being employed to assay the network activation of SC neurons in response to natural echolocation sounds, as well as pure tones and noise bursts. With these population data, we will analyze networks driving stimulus selectivity in complex, natural scenes.

120 Mixed neuronal selectivity to task variables in the mouse somatosensory cortex during recognition of elementary tactile sequences

Michael R. Bale (1), Malamati Bitzidou (1), Elena Giusto (1), Miguel Maravall (1)
(1) Sussex Neuroscience and School of Life Sciences, University of Sussex

Sequential temporal patterning is a key feature of natural signals, used by the brain to decode stimuli and perceive them as sensory objects. To dissect how neuronal activity distinguishes between behaviorally relevant sequential patterns and to begin exploring whether the cortex uses generic mechanisms for sequence recognition across modalities, we developed a GO/NOGO discrimination task in which mice must distinguish between tactile “words” constructed from distinct vibrations assembled in different orders. In the task, tactile sequences can be recognized through several cues, including the arrival of a specific vibration or the presence of transitions between adjacent vibrations.

Adult male mice learned this elementary sequence recognition task after a few weeks of training. Learning also occurred in an auditory version of the task with identically designed stimulus sequences. In the tactile version, animals often responded to the earliest possible cues allowing discrimination, i.e. they effectively solved the task as a “detection of change” problem. However, mice enhanced their performance when collecting sensory evidence or deliberating for longer (30 mice, 122 sessions, Spearman rho = 0.24, p = 0.0083).

Optogenetic inactivation experiments showed that both primary somatosensory “barrel” cortex (S1BF) and secondary somatosensory cortex are involved in the task, consistent with a serial flow of sensory input to decision-making stages. Two-photon imaging in S1BF layer 2/3 of well-trained animals revealed heterogeneous neurons with mixed selectivity to task variables including sensory input, the animal’s decision to lick, and trial outcome (rewards and their departure from prediction). A large number of neurons, even in primary sensory cortex, were activated preceding goal-directed licking, thus predicting the animal’s learned response to a target sequence rather than the sequence itself. These neurons were absent in naïve animals. Therefore, learning generated S1BF neurons that associated the presence of the target sequence with licking, instead of neurons that categorically responded to the sequence or integrated features over time. These results reveal features of cortical activity that sequence recognition shares with other goal-directed sensory discrimination tasks."

121 Auditory processing remains vulnerable to prolonged developmental hearing loss after the critical period

Kelsey L. Anbuhl (1), Todd M. Mowery (2), Dan H. Sanes (3)
(1) New York University
(2) New York University
(3) New York University

Experimental studies of developmental hearing loss (HL) typically focus on a critical period (CP) during which sensory deprivation can permanently disrupt neural function. However, childhood HL often emerges progressively after birth and extends through adolescence, leading to significant perceptual deficits. Furthermore, the magnitude of these deficits increases with longer periods of undetected HL. This suggests that auditory function remains vulnerable to HL after a CP has ended, and implicates HL duration as the key independent variable. Here, we examined the effect of prolonged transient HL (using reversible earplugs) in gerbils, beginning after the auditory cortex CP closes (P23), and extending through adolescence (P102). After earplug removal and restoration of normal audiometric thresholds, animals were trained and tested on an amplitude modulation (AM) detection task using an aversive Go/Nogo procedure. AM depth detection thresholds were measured from psychometric functions 3 weeks after earplug removal (HL group, n=14) and compared to littermate controls (n=12). Auditory brainstem responses were collected to determine whether long duration developmental HL induced changes to the auditory periphery. Following behavioral testing, auditory cortex (ACx) brain slices were obtained from a subset of behaviorally tested animals (control: n=5; HL: n=5) to assess synaptic and intrinsic firing properties in layer 2/3 pyramidal neurons.

Auditory task acquisition did not differ for control and HL animals, with both groups requiring a comparable number of trials to reach criterion performance (i.e., d’ > 1.5 for 100% AM depth). However, HL-reared animals displayed significantly poorer AM detection thresholds, and this deficit persisted through 10 consecutive testing days. Whole cell recordings from ACx pyramidal neurons revealed that excitatory postsynaptic potential (EPSP) amplitudes were elevated in HL animals, while inhibitory postsynaptic potential (IPSP) amplitudes were unchanged, as compared to controls. Furthermore, the threshold current required to evoke an action potential was significantly lower in HL cells, suggesting that ACx cells are more excitable to afferent stimulation. This phenotype is quite different from that observed following HL during the CP which induces a significant reduction of IPSP amplitude and decreases excitability. Taken together, these results reveal that prolonged developmental HL beginning after the CP can induce unique changes to ACx cellular properties, and this may contribute to auditory perceptual deficits."

122 Neural representations of birdsongs across distinct processing regions of auditory cortex

Jordan M. Moore (1), Shihab A. Shamma (2), Sarah M.N. Woolley (1)
(1) Columbia University
(2) University of Maryland

Vocal communicators rely on auditory perception to extract social information from the environment. For example, songbirds recognize conspecifics, tutors, and mates based on the acoustic features of songs. The encoding of these vocalizations in auditory cortex is hierarchical; spike rates in each successive processing stage are progressively more selective for salient sounds. However, it is unknown to what extent changes in auditory coding across regions impact the neural representation of vocal sounds. Moreover, it is unclear if coding specializations in auditory cortex extend to the specific properties of learned stimuli, such as the tutor song. A common approach to quantifying coding specializations is to measure neural tuning for specific acoustic features in vocal sounds, but this method suffers from a bias toward parameters selected a priori and failure to isolate correlated features. Here, we used a stimulus reconstruction method that eliminates these limitations to determine how well song features can be recovered from evoked auditory cortical responses. In zebra finches (Taeniopygia guttata), we recorded the spiking activity of single neurons in the four major regions of auditory cortex (intermediate, superficial, deep, secondary) in response to 15 songs from 3 species. First, we clustered single-neuron response patterns according to their temporal profiles and found that the number of cell clusters increased in successively higher areas of the network hierarchy. Second, we examined whether neural responses could reconstruct conspecific songs more accurately than the songs of two closely related species. Third, we tested whether the neural representation of tutor song differed from those of other conspecific songs in each region. Reconstruction of individual songs from cortical activity revealed circuit-level transformations in coding specificity for species and tutor song in the auditory cortex.

123 Amodal Neural Representations in the Human and Macaque Brain

Ross S. Muers (1)*, Zsuzsanna Kocsis (1,2)*, Catherine Perrodin (3), Christoph Kayser (4), Hiroto Kawasaki (2), Lizabeth Romanski (5), Timothy D. Griffiths (1,2), Matthew A. Howard III (2) & Christopher I. Petkov (1)
(*RSM and ZK joint first authors)
(1) Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, United Kingdom
(2) Department of Neurosurgery, University of Iowa, Iowa City, Iowa, United States
(3) Institute of Behavioural Neuroscience, UCL, Bedford Way, London, United Kingdom
(4) Cognitive Neuroscience, Bielefeld University, Bielefeld, Germany
(5) University of Rochester Medical Center, New York, United States

Amodal representations are those associated with unique entities that are consistent across any form of sensory input (e.g., hearing the voice of an individual, seeing their face or both). Such representations are important for forming abstract concepts. A dominant hypothesis is the “hub-and-spoke” model, whereby modality-specific information from sensory cortices (“spokes”) feeds into modality invariant convergence sites (“hubs”). However, the neurophysiological bases for amodal representations are unknown, and we examined the hypothesis that neural amodal representations are distributed across sensory and higher order cortices. We studied neural responses in intracranial recordings from both human epilepsy patients being monitored for epilepsy treatment and macaque monkeys. The participants were presented with dynamic auditory, visual, and audio-visual stimuli. Recordings in both species were from several fronto-temporal cortical sites along the auditory cortical processing hierarchy. Amodal responses were identified using a vector similarity analysis in the monkey and human local-field potentials (LFPs) as well as single-unit neuronal spiking responses. The Euclidean distance between all combinations of auditory, visual and audio-visual stimuli was cast as a vector and converted to a normalised Amodal Similarity Index (ASI). A response component was categorised as amodal if the ASI value was $<5\%$, indicating a high level of similarity across all stimulus combinations. Time-frequency based analyses showed a substantial proportion of recording sites broadly distributed throughout regions of the temporal lobe that displayed amodal responses in both species. However, the time-frequency patterns were strikingly different between sites with regards to the timing and prominence of amodal response components, e.g., LFP gamma or lower frequency ranges. Amodal responses were also present at the single-unit level but at a lower prevalence. In conclusion, amodal representations in human and monkey intracranial neural recordings appear to be more broadly distributed than suggested by the “hub-and-spoke” model and are differently reflected in neurophysiological response patterns in auditory and higher-order cortices.

124 Experience-based changes to corticostriatal GABAA receptor function gates learning

Nihaad Paraouty (1), Todd M. Mowery (1)
(1) New York University

Auditory learning is likely to require multiple brain regions, including auditory cortex. While the role of the auditory cortex in learning is well studied, that of the striatum, a downstream target of auditory cortex is less clear. To establish the function of the corticostriatal circuit in the acquisition of auditory goal-directed behaviors, we test learning of a Go-Nogo amplitude-modulation rate discrimination task in adult gerbils using an appetitive reinforcement operant conditioning procedure.

First, we show that suppression of the excitatory projections of layer 5 auditory cortex cells to medium spiny cells in the striatum using Designer Receptors Exclusively Activated by Designer Drugs (DREADDS, AAV CamKII HM4D mCh) prevents learning of the task. To assess the changes in synaptic properties during learning, we use a functional corticostriatal slice preparation. Behavioral performance (dprime) was measured and compared to the experience-based changes in inhibitory receptor strength (IPSP, GABAA amplitude). As learning occurs, IPSP amplitude temporarily decreases in striatal cells before returning to baseline values.

To test the idea that a lowering of striatal inhibition is crucial for learning to occur, we infused a GABAA agonist (zolpidem) in the dorsolateral auditory striatum prior to behavioral training to maintain a constant increased level of inhibition. Surprisingly, those animals took a similar number of behavioral training sessions to learn the task as saline-infused controls. We therefore tested zolpidem sensitivity of striatal cells as the animals were learning the task. In vitro recordings reveal that as learning occurs, GABAA receptors in the striatum become insensitive to the drug. This suggests that the ubiquitous removal of mature GABAA alpha 1 subunit containing GABAA receptors from the synaptic membrane plays a key role in procedural learning.

We also tested both the behavioral performance and striatal synaptic properties of a group of animals who had experienced a transient period of developmental hearing loss during the critical period. The hearing-loss animals learned the task at a similar rate as the normal-hearing group. However, baseline IPSP amplitude in striatal cells was significantly lower in hearing-loss animals and learning was accompanied by a transient increase in IPSP amplitude. Direct comparison between the two groups showed that synaptic inhibitory strength moved towards a similar range of synaptic function during learning.

Together, the results suggest that 1) the corticostriatal pathway is crucial for procedural learning of an auditory discrimination task in adult gerbils, and 2) transient changes in striatal inhibition accompany learning, through endo or exocytosis of mature GABAA receptors to a specific functional range. This form of meta-plasticity that permits transient periods of synaptic modifications may support a general mechanism for learning."

125 Observational learning without visual cues

Nihaad Paraouty (1), Joey Charbonneau (1), Dan H. Sanes (1)
(1) New York University

The ability to learn through observing the experiences of a conspecific during development is critical to the emergence of some adult behaviors (e.g., filial imprinting). Typically, observational learning depends on visual and social cues. However, in some natural environments where parents or siblings may serve as demonstrators, observational learning is likely to occur in the absence of sufficient light for the transmission of visual cues. In particular, many rodent species, including the Mongolian gerbil (Meriones unguiculatus), spend much of their lives in underground burrows and are most active at night. Here, we tested the idea that naïve observer gerbils acquire a sound discrimination task by monitoring a demonstrator in the absence of visual cues. Observers acquired the auditory task at a significantly faster rate, as compared to controls that experienced only a cage mate that was not performing the task. Furthermore, the rate of task acquisition was not better when observers were given access to visual cues, suggesting that non-visual information was sufficient for task acquisition. Finally, to assess the social requirement, observers were exposed to experimenter-triggered trials in the absence of a demonstrator. Here, the rate of task acquisition was delayed compared to demonstrator-exposed animals. Taken together, these results suggest that observational learning may occur through monitoring of non-visual cues and is facilited by social experience.

126 Disruptions of learning, memory and experience-induced auditory cortical plasticity in a Next-Generation rat model of Alzheimer's Disease

Andrea Shang (1), Sean Tsaur (1), Sooraz Bylipudi (1), Marc Tambini (2), Luciano D'Adamio (2), Kasia M. Bieszczad (1)
(1) Rutgers University -- New Brunswick
(2) Rutgers University -- Newark

There is a strong link between auditory function and cognitive decline. Hearing loss in midlife has been identified as a risk factor for progression to Alzheimer's disease (AD) (Livingston et al., 2017), and central auditory processing disorders can precede AD onset by 5-10 years (Iliadou et al., 2003), which posits auditory function as a possible early biomarker for later-life progression to dementia. While the primary auditory cortex (A1) is a key site for learning-dependent sensory neuroplasticity that contributes to long-term memory formation, the relationship between auditory system function and cognition remains largely understudied in animal models of AD. Here, we used a next-generation model (NexGenMo) of AD developed by Luciano D'Adamio to examine auditory cognitive function and cortical plasticity in a CRISPR-mediated point mutation knock-in (KI) rat. KI introduces one (App S/H; n = 6) or two copies (App S/S; n = 6) of a familial Swedish mutation to the amyloid precursor protein (APPSwe), vs. controls with the humanized sequence knocked-in (App H/H; n=6). Animals were trained on a 2-tone associative/auditory discrimination (2TAD) task, which requires them to respond (by barpress; BP) to one tone (5.0 kHz) for reward, and to inhibit BPs to another tone (11.5 kHz). Successful auditory learning and cue-selective memory formation has been shown to depend on learning-induced A1 plasticity that sharpens and strengthens acoustic representation of learned cues in long-term memory. We hypothesized that APPSwe would produce disrupted learning and memory due to failures of normal learning-induced cortical plasticity. 2TAD learning and performance levels were delayed and blunted in animals with APPSwe. Memory Tests immediately after reaching performance level criterion also revealed that the memory formed for the rewarded tone was less precise with APPSwe. Another Memory Test 5 weeks later showed that time-dependent consolidation processes that sharpen auditory memories were also disrupted with APPSwe. Electrophysiology revealed normal auditory brainstem responses (ABRs) and cortical physiology to support that learning deficits were not due to hearing loss or atypical A1 organization. However, learning-induced A1 tuning bandwidth changes were different between genotypes and paralleled the learning and memory delays with APPswe. This is the first report on the behavioral and neurophysiological consequences of this NexGenMo of AD on auditory associative learning, and the first of few studies examining memory-related sensory cortical function in AD.

127 Neural circuits for somatosensory control of auditory thalamo-cortical processing

Michael Lohse, Johannes C. Dahmen, Victoria M.Bajo, Andrew J. King
University of Oxford

Considerable attention has been focused on the involvement of cortical areas in multisensory processing. Although visual and somatosensory influences on auditory responses can arise via direct corticocortical pathways, it is likely that some aspects of multisensory cortical processing are inherited from the thalamus. In recent years, the thalamus has received renewed interest, and several studies have suggested that sensory processing at this level may be dependent on a range of contexts, often guided by cortico-thalamic feedback. However, very little is known about the neural circuits that might implement multisensory interactions at the level of the thalamus. We have investigated this by examining the circuitry underlying the influence of tactile inputs on processing in the auditory thalamus in mice.

Our in vivo electrophysiological recordings demonstrated that the mouse auditory thalamus as a whole is influenced by stimulation of the whiskers in diverse, but pathway-specific ways, with primary auditory cortex inheriting signals from the thalamus that are divisively scaled by whisker stimulation. This somatosensory suppression is dependent on a primary somatosensory corticofugal projection and is at least in part implemented via neurons in the higher-order auditory midbrain receiving input from somatosensory cortex. Furthermore, we demonstrate the presence of a parallel direct cortico-thalamic pathway from primary somatosensory cortex to the medial sector of auditory thalamus, which is capable of driving spiking activity and facilitating auditory responses.

Together, these results reveal a previously underappreciated role for auditory thalamus in the implementation of multisensory processing, and the circuits which allow for such thalamic multisensory interactions.

128 Effects of arousal on population coding of natural sounds in primary auditory cortex

Charles R. Heller (1), Daniel Saderi (1), Zachary P. Schwartz (1), Stephen V. David (2)
(1) Neuroscience Graduate Program, Oregon Health and Science University
(2) Oregon Hearing Research Center, Oregon Health and Science University

Behavioral state variables such as arousal, task-engagement, and attention have been shown to decrease shared variability, i.e., stimulus-independent, pairwise correlations between neurons, in primary sensory cortices. This change may reflect state-dependent processing that removes noise and enhances faithful sensory encoding. However, many questions remain regarding the origin of shared variability and how, or if, it impacts sensory encoding accuracy at the population level. Here, we investigated the origin of shared cortical variability and its dependence on arousal state in the primary auditory cortex of awake, passively listening ferrets. The simultaneous activity of multiple single units was recorded during the presentation of natural sounds and arousal levels were monitored via pupillometry. We found that arousal influences correlated variability on multiple, distinct timescales. Consistent with the time course of fluctuations in arousal itself, we observed strong covariation in spike rate from trial to trial, on the order of seconds. This result was expected, given previous work showing that arousal modulates the excitability of cortical neurons. At these slow timescales, we saw no change in the magnitude of shared variability between high and low arousal states. On timescales faster than one second, however, heightened levels of arousal suppressed shared variability. Notably, the degree of suppression for a given pair was not predicted by tuning similarity. Given previous theoretical work showing that shared variability impairs sensory encoding only when present in co-tuned neurons, our results suggest that arousal dependent reductions in shared variability do not necessarily improve sensory encoding. To test this prediction, we compared population decoding accuracy during high and low arousal states. We found that while decoding accuracy improved during high arousal states, this change was primarily attributable to changes in single cell gain and reliability, not decorrelation.

129 Neural correlates of tone-sequence awareness probed with pre- and post-stimulus cues in human listeners

Kai Gaertner, Alexander Gutschalk
University of Heidelberg

Previous studies suggested that a long-latency negativity in auditory cortex is closely coupled to perceptual awareness of tones under informational masking, hence termed the awareness-related negativity (ARN). An alternative interpretation of this ARN is that it reflects enhanced processing subsequent to the detection of the pre-defined target. To further explore the role of the ARN, we present two MEG experiments in which the target can only be identified based on a cue presented before or after the multi-tone scenes.

In Experiment 1, scenes comprising 9 different, non-synchronous tones, each repeated 5 times with random inter-tone intervals, were presented to 20 participants. The target tone was indicated by a cue that was either placed before or after the scene, and participants were asked to indicate if the tone was part of the scene or not. Hit rates were significantly higher (96% vs 76%) and false-alarm rates lower (4% vs 16%) for pre- compared to post-stimulus cues. MEG showed no difference between hit and miss trials for the post-stimulus cues, but strong enhancement of negative source activity in auditory cortex for hit trials in the pre-stimulus cue condition (75-275 ms).

In Experiment 2, to ensure that listeners perceived the whole target stream, random tone sequences (“melodies”) were presented in the presence of a random multi-tone masker to 14 participants. Participants were required to indicate if the post-stimulus cue (a repetition of the target sequence or another random tone sequence) was present in the masker interval, or not (hits: 47%, false alarms: 7%). MEG results in Experiment 2 showed stronger negative source activity in auditory cortex for hit compared to miss trials, despite the post-stimulus cue used.

These results suggest that the ARN may be related to the perception of auditory streams in the presence of a multi-tone masker, but make it unlikely that it is related to the perceptual awareness of the single tones. Possibly, attention is generally required to perceive auditory streams in this setting.

130 Acoustic precision in memory is predicted by learning-induced auditory cortical and subcortical neurophysiological plasticity

Elena Rotondo (1), Kasia Bieszczad (1)

(1) Rutgers, the State University of New Jersey

Despite identical learning experiences, individuals differ in the memory formed of those experiences. Memory formed with acoustic specificity determines its utility for selectively cueing subsequent sound-driven behavior, even in novel situations. If an individual forms generalized memory, then there is potential for novel sound cues to interfere with accurate behavioral performance. Here, a rodent model of auditory learning capitalized on individual differences in learning-induced auditory neuroplasticity to identify and characterize neural substrates for sound-specific (vs. general) memory of the training signal's acoustic frequency. Animals with signal-"specific" memory revealed behaviorally, exhibited signal-specific neurophysiological plasticity in auditory cortical and subcortical evoked responses recorded outside of the training context, indicating that response changes were stable and long-lasting. Learning-induced changes were not detected in animals with "general" memories. Individual differences validated this brain-behavior relationship, such that the degree of change in subcortical (r=0.89, p=0.0002) and cortical (r=0.67, p=0.017) neurophysiological responses predicted the precision of memory formation; cortical and subcortical effects were themselves correlated (r=0.838, p=0.0024). Further, manipulating a histone deacetylase (HDAC3) during memory consolidation was found to promote memory with acoustic precision, resulting in a significant shift along a natural continuum of individual variability in memory formation towards greater acoustic specificity. HDAC3 manipulation enabled precise memory with the same characteristic neurophysiological substrates of auditory memory as untreated, "naturally"-learning subjects. Therefore, this work moves towards an understanding of the of the links between the neurophysiological and molecular substrates of discriminative long-term auditory memories in the auditory system, with implications for feature-specific memory in sensory systems as a whole.

131 Long lasting contextual discrimination in non primary auditory cortex

Mateo Lopez Espejo (1,2), Stephen V. David (1) "

(1) Oregon Hearing Research Center. Oregon Health and Science University.

(2) Neuroscience Graduate Programe. Oregon Health and Science University

Natural sounds are characterized by rich temporal dynamics. In speech, for example, these dynamics span a range of timescales, from fast transitions between phonemes at tens of milliseconds, to slower cadence of words and sentences lasting seconds. While multiple studies have demonstrated that the auditory cortex represents fast temporal features of sound with high fidelity, it remains unknown how slower features are represented. To encode slow temporal features, the auditory cortex must integrate sound information over the relevant time scales. To test for the encoding of slowly varying auditory features, we designed a stimulus paradigm in which a natural probe stimulus was presented immediately following different stimuli that formed distinct contexts. The context could be the naturally contiguous sound, a different natural sound, or silence. Using extracellular recordings from the primary (A1) and non-primary auditory cortex (peri ectosylvian gyrus, PEG) of awake, passively listening ferrets, we characterized how the neural representation of the probe stimulus changed as a function of context. We quantified the amplitude and duration of the context effect over the probe by calculating the pairwise difference between the peristimulus time histogram (PSTH) response to a single probe after different pairs of contexts. In A1, the context-dependent difference rarely lasted more than 50 ms, but in PEG the effect ("memory" of the preceding context) lasted several hundred milliseconds in some neurons. In particular, same-sound contexts typically produced relatively weak responses to the probe, while transitions from silence or a different natural sound produced a much larger response. Thus, our results indicate that long-lasting contextual effects emerge at the single-unit level in non-primary auditory auditory cortex.

132 Competing stimuli in the owl's auditory space map - Evidence supporting a population vector readout

Roland Ferger (1), Michael V Beckert (1), Keanu Shadron (1), Andrea Bae (1), Brian J Fischer (2), Jose L Pena (1)
(1) Albert Einstein College of Medicine
(2) Seattle University

The map of auditory space in the owl's midbrain supports accurate sound localization. Ensemble activity and network architecture in this map has been postulated to represent natural statistics, conveyed to behavioral commands through a population vector (PV) readout of the map, which approximates Bayesian statistical inference. We have previously shown that population response profiles match the conditions for a PV readout. Here we present evidence supporting that a PV based model for the readout of the owl's midbrain auditory space map also works when competing auditory stimuli are presented. We performed multi-electrode array (MEA) recordings of responses in the owl's optic tectum to binaurally presented auditory stimuli – conveying sound localization cues such as interaural time difference (ITD). A decoder based on the PV readout model was used to estimate the stimulus ITD from single trial responses of recorded sub-populations. When two stimuli with different ITDs (i.e. from different directions) were presented, the population vector pointed towards one of the sound sources. This could not be predicted by a simple addition of activity evoked by each stimulus alone. Rather, which stimulus direction is represented by the population depended on the relative saliency of competing stimuli. Both stimulus level and onset timing were used to manipulate saliency. Our decoder was capable of estimating the ITD of the louder sound in a competing stimulus condition (simultaneous onset). This shaping of the population response is consistent with a global inhibition network recently discovered. When two stimuli are presented with slightly different onset times (equal levels), the expectation is that the leading stimulus would also be more salient and, thus, determine the direction represented in the population response. All together, these results show that the PV model can perform accurate localization in complex auditory scenes.

133 The effect of anticipated cue reliability on neural adaptation and novelty detection in barn owls

Keanu Shadron (1), Roland Ferger (1), Jose L Pena (1)
(1) Albert Einstein College of Medicine

The brain actively updates the representation of the environment. An open question about this function is whether adaptation is weighted by the predicted statistics of sensory information. Here we asked whether anticipated cue reliability affects the rate of adaptation in the auditory system of the barn owl.
The midbrain of the barn owl contains a map of auditory space, which uses the interaural phase difference to compute sound location in azimuth. Previous work showed that space-specific neurons in this map are tuned to the frequency range that is most reliable for its preferred location. This effect is due to the acoustical properties of the head, causing higher frequencies to convey interaural phase difference (IPD) more reliably in frontal space and lower frequencies in the periphery in the presence of concurrent sound. We hypothesized that adaptation would be optimized for anticipated reliability, thereby causing a bias in cases of expected low reliability. We also sought to determine if this would lead to a similar bias in novelty detection, where adaptation has been implicated as a potential mechanism. We measured the pupillary dilation response, an orienting response that adapts upon repetition of a stimulus and readily recovers when novel stimuli are presented. Tones of different frequencies and IPD were repeatedly presented to awake barn owls through earphones. This approach was used to assess whether PDR adaptation was correlated with anticipated IPD reliability despite actual IPD reliability being unchanged in sounds delivered through earphones. To assess the strength of the novelty detection, a deviant in auditory location was then presented to elicit a recovery of the PDR. We found that novelty detection was more robust when the anticipated reliability was higher. To assess this question at the neural-population level, we conducted recordings of multiple midbrain neurons using a microelectrode array. Adapter and test stimuli were used to assess population and activity and tuning of individual cells before and after adaptation. Frontal and peripheral neurons were compared to test the hypothesis that anticipated reliable and unreliable stimuli lead to different adaptation rates. Our preliminary results suggest an effect of anticipated statistics on sensory adaptation.