

APAN 2008 ABSTRACTS

Contextual effects in neuronal responses to complex acoustic stimuli differ between areas A1 and AAF

Misha B. Ahrens (1), Jennifer F. Linden (2) and Maneesh Sahani (1)

(1) *Gatsby Computational Neuroscience Unit, and (2) Ear Institute and Dept. of Neurosci. Physiol. and Pharmacol., University College London, London, United Kingdom*

The primary auditory cortex (A1) and anterior auditory field (AAF) are both thalamo-recipient "core" auditory cortical areas, distinguished from each other by a reversal in tonotopy. When stimulated with complex dynamic sounds, neurons in mouse A1 and AAF exhibit different linear filtering properties as assessed through analysis of spectro-temporal receptive fields (STRFs) (Linden et al., *J Neurophysiol* 90:2660, 2003). Generally, A1 filters are slower, and more broadly tuned, than those in AAF. We have recently proposed a new way to characterise auditory cortical response properties (Ahrens et al., *J Neurosci* 28:1929, 2008) with models that incorporate the nonlinear effects of short-term acoustic context. These models identify a "context receptive field" (CRF) that modulates the efficacy of spectrotemporal elements within the stimulus before integration by the STRF. Many contextual effects, including phenomena previously probed only with simple stimuli (such as forward suppression and combination sensitivity), can be captured for a complex acoustic stimulus with the CRF. Here we compare the properties of the CRFs identified from responses of cells in A1 and AAF to dynamic random chord stimuli. We find that: (1) CRFs in both A1 and AAF are typically inseparable (the predictive power of the inseparable context model, i.e. the fraction of explainable variance explained by the model, was between 0.40 and 0.77 across both areas, with a jackknife estimate of 0.63, which is considerably higher than the values previously reported for separable context models in Ahrens et al., 2008); (2) CRF modulation is larger in A1 than AAF (maximum modulation of average CRF in normalised units: 0.92 in A1 against 0.85 in AAF); (3) spectral interactions within the CRF appear to be strongly asymmetric in A1, but less so in AAF; (4) in line with the properties of the STRFs, contextual effects in A1 are slower and longer-lasting than those in AAF (half-peak delay of average CRF: 120 ms in A1 and 80 ms in AAF). These findings show that the nonlinear effects of acoustic context differ between AAF and A1 neurons. In combination with previous results, they suggest that AAF may be specialised for rapid, temporally and spectrally precise processing, while A1 neurons integrate more broadly along both spectral and temporal dimensions.

Late-deafness induces massive crossmodal reorganization of ferret auditory cortex.

BL Allman, LP Keniston and MA Meredith

Department of Anatomy and Neurobiology, Virginia Commonwealth University School of Medicine, Richmond, VA, USA

Congenital deafness is known to induce the crossmodal reorganization of auditory cortical structures, but if the loss occurs after sensory maturity has been established, the extent of crossmodal reorganization adult animals is largely unknown. The present experiments examined the possibility of crossmodal reorganization in the auditory cortex of ferrets deafened well after the established age at which tonotopic organization and representation of inputs from each ear reach maturity (~60 days old). Six ferrets (150±34 days old) were deafened (>90 dB threshold) using a kanamycin/ethacrynic acid protocol. Approximately 70 days elapsed after deafening before single unit extracellular recordings were made in the auditory cortex (AAF, A1, ADF, PPF and PSF), with an emphasis on the core auditory fields (AAF and A1). Of the 225 neurons studied in 69 penetrations in the deaf adults, none were responsive to acoustic or visual stimulation. Instead, 188 neurons (84%) were reliably activated by somatosensory stimulation, most often through hair receptors on the face, head and neck, and the somatosensory receptive fields were almost exclusively bilateral (92%). In a separate set of experiments, recordings in the core auditory fields (AAF and A1) of 4 untreated, hearing adults revealed that almost all of the neurons (96%; n=100/104; 10 penetrations) were responsive to auditory stimuli, with none of these neurons responsive to somatosensory stimulation. These data demonstrate

that late-onset deafness can induce massive crossmodal reorganization across the entire auditory cortex. Supported by NIH Grant NS39640.

Selectivity for natural sounds in the auditory forebrain is strongly shaped by the acoustic environment

Noopur Amin and Frederic E. Theunissen,
U.C. Berkeley

Perceptual discrimination of vocal communication signals is crucial for the reproductive fitness of many animals in the wild, including birds. We have investigated and found support for the postulate that the avian auditory system shows some degree of specialization for the processing of species-specific vocalizations. Neural responses in the zebra finch auditory forebrain regions of field L and the lateral caudal mesopallium (CLM) have shown selectivity for conspecific song compared to statistically-matched synthetic sounds (Grace et al., 2003). Here we investigate the role that structured acoustic stimulation during development plays in shaping this neural selectivity for natural sounds: we raised zebra finches in isolation and in continuous unstructured white noise until adulthood and then electrophysiologically recorded responses in field L and CLM to natural sounds and matched synthetic sounds. We then compared the neural selectivity obtained from birds raised in noisy environments to the results obtained from normal, social adults. We find that the selectivity for conspecific song is drastically reduced when compared to a subset of synthetic sounds and completely disappears when compared to more broadband type synthetic sounds. This is the first evidence that absence of patterned auditory stimulation during post-natal life dramatically reduces the neural selectivity for natural sounds. Our study also reveals that tuning to power spectra found in natural sounds is mostly unaffected, whereas the tuning to the fine structure of natural sounds (i.e. temporal and spectral modulations found in song) is either acoustically and socially driven or at the very least sensitive to environmental and social manipulation. Our findings also imply that impoverished or noisy environments have a powerful impact on the brain and could adversely affect important perceptual tasks.

Temporal envelope coding and decoding in the inferior colliculus

Sharba Bandyopadhyay¹, Paul C. Nelson², Zachary M. Smith³ and Eric D. Young²

¹ *Institute for Systems Research, University of Maryland, College Park*

² *Department of Biomedical Engineering, Johns Hopkins University, Baltimore*

³ *Research and Applications, Cochlear Americas, Englewood*

Temporal envelope coding properties of neurons are usually studied through measures like modulation transfer functions (MTFs) and spike-triggered averages (STAs) of the stimulus envelope. In general, such measures are biologically relevant only if later-stage neurons are capable of reading information encoded in such explicit formats. This study investigates both coding and extraction of temporal envelope information in responses of inferior colliculus (IC) neurons in the awake marmoset to stimuli with random fluctuations imposed on their envelopes. These stimuli have a tone carrier (usually at the best frequency of the neuron) modulated by an m-sequence. We use a general spike-time based distance metric developed by Victor and Purpura (VP-metric) to quantify the information in the responses about the envelope. This metric implies a biologically realistic decoder (a coincidence detector), but makes no assumptions about encoding or the forward representation. The representation of coding of stimulus envelope with MTFs or STAs implies an optimal linear decoder to read the information encoded in these forward representations. Using the optimal linear decoder we compute the information present in the forward representation. By comparing the two, in the form of mutual information between stimulus and response, we ask the question: how good are such representations compared to a general spike time based nonlinear decoder that implements the VP-metric? We find that often the optimal linear decoder captures as much information as the VP-metric based decoder, suggesting sufficiency of the linear forward representation, especially for IC neurons that otherwise respond linearly to stimuli (type I neurons). Using 100-millisecond stimulus and

response epochs, most neurons have close to the maximum possible mutual information, suggesting complete discrimination of these segments by single neurons. Finally, we compare the amount of envelope information present in responses of these IC neurons over different stimulus lengths to that available in the responses of model auditory nerve fibers to study transformations of envelope coding between the two stages. (Supported by NIH-NIDCD grants DC00115 and DC009164)

Dynamic Range Preservation by Auditory Neurons

Dennis L. Barbour, Paul V. Watkins

Department of Biomedical Engineering, Washington University, St. Louis, MO, USA

Increases in stimulus intensity typically elicit increases in spiking rates for sensory neurons. These monotonic input/output functions are able to represent stimulus intensity unambiguously because over the dynamic range of the neuron, each possible spiking rate corresponds to a single intensity (i.e., the function is invertible). Neurons in the auditory periphery universally demonstrate this property, but central auditory neurons commonly respond nonmonotonically as a function of the level of sound stimuli, such that these neurons appear to be tuned to sound level. Nonmonotonic input/output functions reflect an ambiguous coding strategy because each output rate corresponds to two input intensities. The coding significance of such functions is unclear. Neurons have the ability to adapt their input/output functions to improve coding accuracy, and we exploited this property in order to explore which portion of level-tuned neurons is used to encode sound. Our results imply that auditory responses previously thought to represent level tuning may actually reflect a two-part coding strategy: the positive slope of such functions is used to encode the lowest sound levels in much the same way as monotonic input/output functions do for somewhat higher intensities; the negative slope, however, may function to preserve this high sensitivity when relatively rare but intense events occur that desensitize monotonic functions temporarily. These findings provide critical insight into how sensory systems can maintain sensitivity over wide dynamic ranges with both rapid and slow changes in stimulus statistics.

Representation of amplitude modulation envelope in the marmoset auditory thalamus

Edward L. Bartlett¹ and Xiaoqin Wang²

(1) Purdue University (2) Johns Hopkins University

Representation of the sound envelope is essential for accurately decoding speech, animal vocalizations, and other natural sounds. Not only is the rate of envelope modulation important, but the contour of amplitude modulation can serve as a reliable way to discriminate sounds that are modulated at the same frequency. There is evidence that different neuron types in the cochlear nuclei are specialized for representing the modulation frequency and the envelope shape in their responses. Furthermore, different regions of the auditory cortex demonstrate preferences for representing slowly and rapidly modulated envelopes by stimulus-synchronized and non-synchronized discharges, respectively. Auditory cortex neurons are also sensitive to envelope shapes even when modulation frequencies are identical. It is not known whether neurons in the auditory thalamus, which provides the sensory input to auditory cortex, have response characteristics that are more similar to neurons in auditory brainstem nuclei or auditory cortex. We studied single-units in the auditory thalamus of awake marmosets in response to sinusoidally amplitude-modulated (SAM) stimuli with tone or noise carriers, as well as tone pips shaped by Gaussian envelopes. Units were recorded from four subdivisions of auditory thalamus. Synchronized thalamic responses to SAM stimuli could be separated mainly into two populations depending on how closely they followed the sinusoidal envelope contour. Responses that followed the modulation contour were more common at slower modulation frequencies (> 8 Hz) and in the anterodorsal and ventromedial subdivisions. At higher modulation frequencies, responses for which spikes only occurred during a small portion of the stimulus cycle were common in the ventral and anterodorsal subdivisions. Neurons in the caudodorsal division showed selectivity for modulation frequency but typically had broad, weakly synchronized responses or produced selectivity only by changes in firing rate. At slower modulation frequencies, responses to SAM noise stimuli diverged

significantly more from the envelope contour than SAM tone stimuli. The sensitivities of individual neurons to carrier type varied widely. Our results indicate that individual neurons are sensitive to specific combinations of modulation frequency, envelope shape and carrier type, enabling a small population of neurons to uniquely specify the amplitude modulation for a given carrier. Models of forebrain temporal processing must consider additional relevant parameters along with modulation frequency. *Supported by: NIDCD DC03180 (XW) and DC06357 (ELB) and the Deafness Research Foundation (ELB)*

Characterisation of the BOLD response in the auditory system of non-human primates

S. Baumann, T.D. Griffiths, D. Hunter, L. Sun, A. Thiele

Institute of Neuroscience, Newcastle University

This study examined the fMRI BOLD response to auditory stimulation in primates to test the hypothesis that this is different in primary and non-primary cortex, suggested by human work (Seifritz et al., 2002). The data were acquired using a paradigm that can be applied to both humans and primates to allow comparison of the responses in homologous areas.

fMRI BOLD responses at 4.7T were recorded from two rhesus monkeys (*maccaca mulatta*) during stimulation with broadband noise (25-16000 Hz) at an rms level of 80 dB SPL. Frequency mapping was used to define volumes of interest corresponding to the three core and adjacent belt areas. The temporal dynamics of the haemodynamic response function (HRF) to the sound were assessed following short (2s) and long (8s) stimulus presentations. Interference with scanner noise was avoided by the application of a “sparse sampling” protocol with a repetition time of 18 s and image acquisition time of 1 s while a high temporal resolution of 1s was maintained through temporal jittering of the sound stimuli in respect to the image acquisition.

Significant activation in response to the sound was observed bilaterally in the inferior colliculi, thalamus, and core and belt areas of the auditory cortex (Fig. 1). The spatial location of the observed maxima in response to sound remained very stable from session to session. The detailed time course of the HRF signal was different in brainstem, core and belt areas, in patterns that were conserved between sessions. In all areas, the maximum of the percent signal change was observed between 2 – 5 s after sound onset for the 2 s sounds and later for the 8 s sounds.

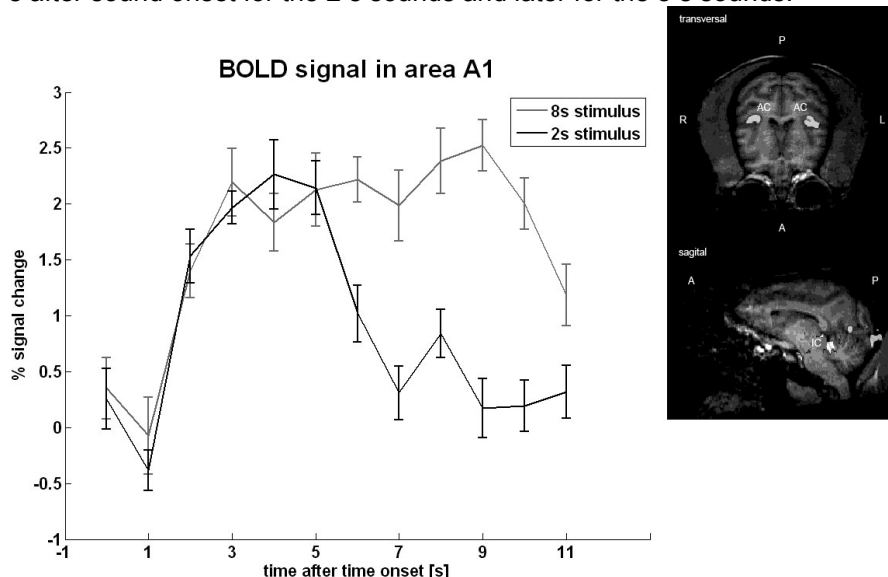


Figure 1: Example time courses for two stimulus durations from a single session in one monkey derived from the primary auditory cortex. Figure inlet shows significant auditory activity in the auditory cortex (AC) and inferior colliculi (IC) overlaid on a structural MRI scan.

Seifritz et al. (2002). *Science*, 297(5587):1706-8.

Learning strategies that rely on tone-onset during auditory associative learning predict the development of signal-specific plasticity in A1

K.M. Berla^{*}, N. Gross, & N.M. Weinberger.

Center for the Neurobiology of Learning and Memory and Dept. of Neurobiology and Behavior, University of California, Irvine, CA.

Strategies that animals use to learn have profound implications for the development of associative auditory cortical plasticity (Berla^{*} & Weinberger 2008). A general rule for plasticity could be learning strategies (LS) that make use of the natural proclivities of sensory cortical areas, i.e., onset transients in primary auditory cortex (A1), induce plasticity in those areas to subserve learning & memory. Adult rats bar-pressing (BP) during a tone for reward can solve the problem using different strategies. Use of a LS that emphasized on tone-onset produced frequency-specific plasticity in A1: a reduction of threshold and of bandwidth. To achieve complete dependence on the "tone-onset" LS, we trained animals in the same task but also rewarded the first BP after tone-offset. BPs following tone-offset significantly increased, indicating that subjects were ignoring tone offset. Subjects making full use of a "tone-onset" LS developed frequency-specific plasticity in A1 consisting of a doubling of the area representing characteristic frequencies (CF) centered ± 0.25 octave of the signal tone. Therefore, increasing dependence on the use of tone-onset LS induces functional reorganization of A1. This suggests that: (a) learning without tone-specific A1 plasticity reflects "low demand" on A1 to support learning, (b) tone-onset LSs induce tone-specific receptive field modifications without CF-shifts due to "moderate demand" on A1, and finally (c) complete reliance on tone-onset LSs imparts "high demand" on A1 resulting in signal-specific A1 expansion. Overall, the findings show that learning strategies determine specific associative plasticity by capitalizing on the response proclivities of sensory cortex. *Supported NIH(NIDCD), DC-02938 and DC-05592.*

Decoding population activity in Auditory Cortex: neural correlates of pitch perception

J.K Bizley, K.M.M.Walker, A.J. King and J.W.H. Schnupp,

Department of Physiology, Anatomy and Genetics, University of Oxford

Ferrets were trained to judge whether the pitch of an artificial vowel sound was higher, or lower, in pitch than a preceding reference sound. Artificial vowels consisted of click trains, through a cascade of bandpass filters. The click rate determined the pitch. Psychometric performance was assessed across a range of reference pitches and expressed as Weber fractions (Δ pitch/reference pitch).

Extracellular recordings were made, using multi-site silicon probes, in the auditory cortex of anaesthetised and awake, passively listening, ferrets. Stimuli were vowel sounds identical to those tested behaviourally. To examine neural performance, one sound pitch was assigned as the reference with sounds ± 1 octave considered as targets. The responses of single neurons were used to construct "neurometric" discrimination functions, based on a comparison of the spike count elicited in response to reference and target sounds. For some single neurons neurometric Weber fractions matched those observed in trained ferrets. However, single neurons were only capable of "performing the task" only over a very restricted range of reference pitches, and neurometrics of only a small proportion of neurons matched the ferrets' behavioral performance. Given that these sounds evoke activity from many neurons it seems likely that the brain must use the activity patterns across neural populations to solve this task. Population neurometric performance was therefore examined using a pattern recognition algorithm based upon the spike rates of simultaneously recorded neurons ($n=5-50$). Responses were classified according to whether they more closely matched the response to the highest pitch sound, or to the lowest, based upon which was closer in Euclidean space. Neurometrics obtained in this manner almost always exceeded that of the best single neuron within the population. Moreover, population neurometrics performed well across the full range of reference pitches. In order to explore the potential coding strategies available to the brain, we also computed population neurometrics using a relative first spike latency code and a reduced spike code which simply asked whether the neuron fired during a 75ms window following stimulus onset.

Weber fractions calculated for individual populations of neurons with each of these decoding strategies were very similar. In all three cases, comparisons of neurometric and psychometric performance based on Weber fractions revealed that the best neurometric performance matched, but did not exceed, the best performance measured behaviourally.

Click train responses in the left and right auditory cortex of awake primates

Michael Brosch, Elena Oshurkova, Henning Scheich.

Leibniz-Institut für Neurobiologie, Brenneckestraße 6, 39118 Magdeburg, Germany

We studied neuronal firing during stimulation with periodic click trains in 6 fields of the auditory cortex of two awake longtail macaques. Click trains lasted for 2 s and consisted of click rates that varied between 1 and 300 Hz from trial to trial. Neuronal responses were characterized (1) by the overall rate changes that occurred during the steady state portion of the click train and (2) by the vector strength, reflecting the degree of neuronal synchronization with individual clicks. Multiunit recordings were made from the primary (AI), the caudomedial (CM) and caudolateral (CL) auditory field of the left and the right hemisphere.

We found that the neuronal responses in the 6 fields varied differently with click rate; generally these differences were more pronounced for synchronized than for rate responses. Differences were larger between homologous fields located in different hemispheres than between different fields located in the same hemisphere. Interhemispheric differences were most pronounced in AI and in CM; intrahemispheric differences were most pronounced between CL on the one hand and AI and CM on the other hand. Compared to the right hemisphere, the left hemisphere contained more units that exhibited rate responses and these responses were often stronger. Units in the left hemisphere preferred higher click rates and could respond to higher click rates although their vector strengths were generally lower. Our results suggest different involvement of left and right auditory cortex in the processing of temporally modulated sounds.

Modulation rate tuning of LFPs in macaque auditory cortex: comparison to single unit data

C.R. Camalier¹ and Troy A. Hackett^{1,2}

(1) Vanderbilt Brain Institute (2) Dept. of Psychology, Dept. of Hearing and Speech Sciences; Vanderbilt University, Nashville TN

Functional properties and organization of auditory cortex are being investigated using a wide range of techniques. Minimally invasive methods (e.g., EEG, MEG, fMRI) are favored in human studies and some animal studies, whereas invasive approaches (e.g., single/multiunit, local field potentials) are most commonly employed in animal studies. One way to bridge the gaps between single unit and noninvasive techniques is to utilize the intracranial local field potential (LFP), which is thought to be better correlated with scalp potentials and the BOLD signal than single unit (SU) activity. Towards that end, the purpose of the present study was to better understand the relationship between LFP and (SU) activity in response to temporally modulated sounds. We simultaneously recorded LFPs and SUs from auditory cortex in the awake passive listening macaque. The stimulus battery included amplitude-modulated Gaussian noise with rates ranging from 3 to 251 Hz. Previous work from our lab and others has shown that SUs are tuned in both firing rate change and degree of spike synchrony to the stimulus. Similarly, an analysis of the LFP shows rate-dependent stimulus-locked modulation to these stimuli. The degree of stimulus-locked modulation at different rates can be expressed as a temporal modulation transfer function by characterizing the power spectral density of the signal at a given modulation rate. These data indicate that LFP and SU recordings synchronize to the temporal envelope of complex sounds in a comparable manner. In some cases, the LFP synchronizes to higher firing rates than SUs, possibly reflecting loss of synchrony due to synaptic delay.

Experience-dependent changes in neuronal response properties within the avian telencephalic auditory area field L

E. Caporello T. Q. Gentner

UCSD Neuroscience Program.

The importance of vocal communication and recognition in songbird behavior makes the songbird an ideal model for studying auditory processing. We are currently exploring the effect of experience on the avian telencephalic auditory area, field L. Experience-dependent receptive field changes occur in the homologous mammalian structure, primary auditory cortex, and selectivity is known to develop for behaviorally relevant song in downstream targets of field L. Two training stimulus sets were composed of identical songs with complementary frequency bands replaced with noise. European Starlings (n=2) were trained to discriminate between songs within a training set using a go-nogo behavioral training paradigm. Training sets were counterbalanced between subjects. After the subject reached criterion performance, field L recordings were made under urethane anesthesia. 24 single units and 86 multi units were recorded extracellularly using sixteen-channel tetrode arrays. Within this population of neurons, the mean response to the training set was significantly less than the response to the complementary training set ($p < 0.0001$ T-test), as was the response strength ($p < 0.0001$ T-test). Of the 110 units recorded, 28 units showed significant selectivity ($p < 0.05$ ranksum) for one class of training stimuli, the majority of these (26 of 28) were selective for the complementary training set. These data suggest that frequency specific changes can occur in field L as a result of experience. We are currently exploring the receptive field changes that may be occurring in field L as a result of this frequency-limited training, as well as the relative effects of experience in the subfields of Field L.

Differential information exchange between primary auditory cortex and the anterior auditory field in the cat

Andres Carrasco, Kelly N. Decker, and Stephen G. Lomber

Centre for Brain and Mind, Department of Physiology and Pharmacology and Department of Psychology, University of Western Ontario, London, ON, Canada.

The purpose of the present study was to examine the functional influence that primary auditory cortex (A1) has on the anterior auditory field (AAF) and vice versa. Multiunit recordings were made in the right hemisphere of nine mature cats anesthetized with sodium pentobarbital. Following A1 or AAF mapping using tonal stimuli, a cooling loop was placed over the lower to middle isofrequency bands of A1 or AAF. The neuronal response strength was then measured with tonal stimuli before, during and after deactivation of A1 or AAF. Activity was recorded from sites throughout A1 or AAF including sites with characteristic frequencies either matching or not matching the deactivated region in the adjacent field. Our results show that during A1 deactivation there is a modest reduction of acoustically-evoked activity in AAF, and that the observed decrease in activity was followed by a return to baseline following A1 re-activation. In contrast, deactivation of AAF resulted in a pronounced decrease in acoustically-driven responses in A1. Regardless of characteristic frequency, these changes were consistently identified at sites throughout A1 or AAF. Although these variations in response strength were observed during deactivation of A1 or AAF, we did not find that the deactivations altered the characteristic frequency. Collectively, these results suggest that AAF significantly influences activity in A1, while A1 has only modest influences on acoustic processing in AAF. This indicates that the transcortical flow of acoustic information moves predominantly from AAF to A1, and not from A1 to AAF. *Supported by CIHR and NSERC.*

Functional connectivity underlying evoked inhibition in primary auditory cortex *in vivo*

P Chadderton & KD Harris

Center for Molecular & Behavioral Neuroscience, Rutgers Newark, NJ 07102 USA

Within the neocortex, the sensory world is represented through the concerted activity of large numbers of interconnected neurons. The relationship between the activity of individual cortical cells and neuronal populations is poorly understood, but is likely to be determined by the pattern of inputs

received by synaptically-connected cells. To date, the properties of cortico-cortical synaptic connections have not been explored *in vivo*. Therefore, we have made simultaneous intracellular and extracellular-population recordings from neurons in primary auditory cortex of urethane-anaesthetised rats (P21-28) in order to study the functional network connectivity of single pyramidal neurons. Whole cell recordings were performed simultaneously with 32-site silicon probe recordings (4 shanks, 2 tetrodes per shank), from layer II-V neurons, permitting the sub- and suprathreshold activity of single cells to be directly related to the spiking activity of 20-80 units. Spike-triggered averages of individual extracellular units were generated from voltage-recording and voltage-clamp data. EPSP-like waveforms were observed from small subpopulations (1 to 9) of units in each experiment (n = 10). The onset of EPSP-like waveforms often preceded the incidence of extracellular spikes, indicating a high degree of common input between pre- and post-synaptic neurons. We find that a reliable temporal sequence of activation across extracellularly-recorded pyramidal cells may contribute to a 'compound EPSP' in the intracellularly-recorded neurons, that is driven-directly, or shares common input with a functional distinct subpopulation of cortical cells. In addition, we find that tight synchrony amongst cortical interneurons (cross-correlogram peaks $\leq \pm 5\text{ms}$, n = 10), underlies large all-or-none IPSCs in postsynaptic pyramidal cells during sensory stimulation. Thus presynaptic inhibitory and excitatory neurons contribute via functional subpopulations to shape the output of their targets. *This work was supported by grants from NIH, NSF, and the European Union.*

Dynamic activation and modulation of human neocortex during phonemic reception

Edward F. Chang^{*1,2}, Erik Edwards^{*1}, Noa Fogelson¹, Sarang Dalal¹, Nicholas M. Barbaro², Heidi Kirsch³, Srikantan Nagarajan⁴, Robert T. Knight¹ **First co-authors*

¹*Helen Wills Neuroscience Institute, University of California, Berkeley*

²*Department of Neurological Surgery, ³Neurology, and ⁴Radiology, University of California, San Francisco*

Previous studies have implicated the superior temporal gyrus (STG) in the processing of complex communication sounds such as phonemes. However, how behavioral conditions such as attention and memory affect processing in the STG is unclear despite the important consequences for the dynamic modulation of speech reception. Here, we used direct cortical surface recordings (electrocorticography) in six human subjects to localize phoneme-responsive cortex during the processing of vowel and consonant-vowel phoneme tokens. Time-frequency analyses (Hilbert transform) demonstrated robust yet spatially discrete evoked high-gamma oscillations in the both the posterior and middle portions of the superior temporal gyrus, as well as in the precentral gyrus/premotor cortex. These posterior frontal lobe motor areas co-localized with cortical activity induced during self-paced silent and articulated voicing gestures of phonemes. High-gamma oscillations in both areas were substantially augmented while subjects were engaged in a working memory task. Finally, changes in cortical activity were observed with increasing memory load. These results provide definitive evidence for novel co-activation of motor and auditory cortical areas during passive phonemic reception and their modulation during attentional and working memory conditions, and thus have consequences for prevailing theories of cortical speech perception.

Physiological and anatomical identification of parabelt regions in primate auditory cortex

Poppy A.C. Crum, Elias B. Issa, Troy A. Hackett, and Xiaoqin Wang

Biomed Engin., Johns Hopkins Univ. Sch. Med., Baltimore, MD; Dept. of Hearing and Speech Sci., Vanderbilt Univ. Sch. of Med., Nashville, TN

Anatomical studies of human and non-human primates have suggested that the auditory cortex is divided into hierarchically connected core, belt, and parabelt regions distinguished by both thalamocortical and corticocortical connectivity (Hackett et al, 1998). However, to date there exists little physiological evidence for a similarly defined parabelt region. The paucity of physiological data within this region largely results from lack of reliable *in vivo* indicators of its boundaries. Previously, we reported a new method to address this difficulty by measuring the Current-Source-Density (CSD) to

register a single electrode penetration as belonging within a given cortical region. Post-mortem histological staining (PV, vGlut2, AChE, and Nissl) confirmed a tight relationship between shifting anatomical patterns of lemniscal input and the presence of a defined layer IV current sink in the CSD. Here, we report our first single neuron and local-field-potential (LFP) recordings from three areas, core, belt, and parabelt identified with our new approach that links both anatomical and physiological classification of these regions. Using a single tungsten electrode the LFP was measured at 100 μ steps orthogonal to the laminar striations and used to compute the CSD for an individual recording track. These recordings were made across the medial-to-lateral surface of the awake marmoset auditory cortex. Simultaneously recorded single-units and LFPs were grouped using boundaries estimated from the CSD as originating from the core, belt, or parabelt. Physiological differentiation was observed for both single-units and LFP responses. These included marked changes in latency, bandwidth, and synchronization to modulated sounds. Specifically, both latency and spectral tuning width increased from the core to belt and parabelt whereas the frequency at which cells could synchronize to modulated sounds decreased along the same dimension. These findings provide evidence for a physiologically defined parabelt region and suggest that CSD-based electrode registration offers a useful measure for identifying the location of recorded neural response in the primate auditory cortex as originating from a particular cortical region across the medial-to-lateral dimension.

Control of single neuron activity by sensory stimuli and global network dynamics in auditory cortex

C. Curto, S. Sakata, S. Marguet, K.D. Harris
CMBN (Newark), Rutgers Univ., Newark, NJ

The electrical activity of neurons reflects an interplay of sensory input and the brain's own internal dynamics. In sensory cortices, neuronal firing correlates well with characteristics of sensory stimuli; on the other hand, each cortical neuron receives the vast majority of its inputs from other cortical neurons, suggesting that spiking is largely controlled by the activity of the local network. This viewpoint is supported by simultaneous recordings of multiple cells, which show synchronized patterns of spontaneous activity beyond those imposed by the structure of the sensory stimulus.

In prior work, we found that the global dynamics of population activity in rat auditory cortex is well approximated by a low-dimensional self-exciting system model, and that the variations in population dynamics with cortical state can be captured by changes in the parameters of this model. Here we investigate the relationship of identified single neurons to global population dynamics in this context. In the model, population activity is characterized by a pair of 'mean field' variables, v and w , that reflect the average population firing rate and integrated recent past activity, respectively. To predict the spike times of individual neurons from population activity, we use an approach analogous to the computation of hippocampal "place fields", by predicting the mean firing probability of each neuron as a function of position in the v - w plane, which we term the 'activity field.' We find that activity fields for different neurons are quite localized in distinct regions of the v - w plane. We conclude that, while the mean activity of a column is well approximated by a simple low-dimensional dynamical system, individual neurons show widely different relationships to this dynamics. For any neuron, activity fields computed from spontaneous and sensory-evoked activity were quantitatively similar, further suggesting that the structure of sensory responses reflects the same network dynamics that shape cortical spontaneous activity. *This work is supported by NIH Grant MH073245.*

Neuronal and perceptual adaptation to the statistics of a binaural spatial cue

Dahmen JC, Schulz A, Keating P, King AJ
Department of Physiology, Anatomy and Genetics, University of Oxford, UK

Adaptation phenomena have been reported in all sensory systems and can provide valuable insights into mechanisms of sensory coding. To examine whether the mammalian auditory system adapts to the statistics of binaural spatial cue values, and how adaptation at the neuronal level may translate into perceptual phenomena we recorded from neurons in the inferior colliculus and primary auditory

cortex of anaesthetized ferrets and carried out behavioural experiments in human listeners using almost identical stimuli. Stimuli consisted of a combination of dynamic adapters and static test stimuli. The adapters comprised five-second-long sequences of broadband noise with dynamically varying interaural level differences (ILDs). The ILD values of the adapter were drawn randomly from a Gaussian distribution and changed every 5 ms. Test stimuli were 100-ms-long noise bursts with a static ILD, which were presented immediately after the adapter sequence.

Employing reverse-correlation we characterized each neuron's activity during adaptation in terms of a linear filter and a nonlinear gain function. Responses to the static test ILD were used to obtain more traditional ILD-response functions. During behavioural experiments human listeners were required to lateralize the static test ILDs in a two-alternative forced choice task.

Given a sufficient number of spikes, stimulus-response relationships could be successfully characterized with a linear-nonlinear model for the majority of neurons as evidenced by the model's ability to predict responses to new stimulus sequences with high accuracy. Neuronal adaptation to changes in the mean or variance of the distribution from which ILD values were chosen was closely matched by the perceptual effects observed in human listeners.

The stimulus feature that best drives the majority of neurons is a negative deflection from the stimulus mean, i.e. a relative increase in level in the contralateral ear. This feature preference remains largely constant across changes in the mean of the stimulus distribution as does the sensitivity with which neurons respond to their preferred feature. This feature constancy is also manifest in the shifts of the ILD-response functions constructed from static ILDs. Parallel changes were observed in human perception as lateralization was biased away from the mean of the adapter. Decreasing the variance of the adaptor's distribution was associated with an increase in neuronal gain and steeper ILD-response functions. The psychophysical experiments provided evidence for a perceptual correlate of this increase in neuronal sensitivity as lateralization thresholds improved with decreasing variance of the stimulus distribution.

A dynamic network for enhancing contrast in primary auditory cortex during behavior

Stephen V. David, Jonathan B. Fritz, Shihab A. Shamma

Inst. Syst Rese, Univ. Maryland, College Park, MD

Auditory behavior requires classifying sounds according to spectro-temporal properties and associated meaning. In simple operant conditioning paradigms, one class of sounds (targets) requires an active response while another class (distractors) requires no change in behavior. The prevailing neurophysiological model for such behaviors is that sensory cortex operates as a matched filter, enhancing the responses of neurons that signal targets and diminishing responses of neurons that signal distractors. However, recent studies have shown that additional contingencies, including reward value, motivation and task difficulty, can also modulate sensory cortical responses. To learn more about the influence of task contingencies during sound discrimination, we recorded from neurons in ferret A1 under two different behavior paradigms. Both tasks required detecting a pure tone target in a sequence of broadband noise bursts (temporally orthogonal ripple combinations). The first paradigm (n=111 neurons) used conditioned avoidance: Water reward was automatically delivered during distractors, and subjects were punished with a small shock if they failed to pause drinking after a target. The second paradigm (n=175 neurons) used positive reinforcement: Target hits were rewarded with water, and false alarms were punished with a timeout. Thus both tasks required the same discrimination but associated target and distractor classes with different reward values.

We compared the spectro-temporal tuning properties of single A1 neurons during both tasks and also during passive listening. During conditioned avoidance, the observed pattern of modulation was consistent with existing matched filter models. Neurons shifted their spectral tuning toward the target frequency, and neurons that preferred targets over distractors tended to increase their overall gain. However, preliminary data collected during positive reinforcement showed an opposite pattern of modulation. Neurons instead shifted their tuning away from the target frequency, and target-preferring neurons tended to decrease their overall gain. Our results are consistent with a generalized matched filter model, in which contrast between target and distractor classes is enhanced across the A1 population response but the direction of contrast enhancement depends on motor and reward

contingencies associated with the sound classes.
Support: NIH R01 DC005779, NIH F32 DC008453

Involvement of the Inferior Colliculus in tinnitus

Didier A Depireux, Yadong Ji, Barak Shechter, Elizabeth Powell
Anatomy and Neurobiology, University of Maryland, Baltimore MD 21201 USA

Tinnitus is an often debilitating handicap. Converging evidence points to the central involvement of the inferior colliculus of the auditory midbrain in the development and maintenance of tinnitus. Therefore, in rats equipped with chronic multi-electrode arrays implanted in auditory midbrain, we quantify changes in neural spontaneous activity, excitability and sound coding before and after noise trauma-induced tinnitus, while verifying the presence of tinnitus through a behavioral assay and the auditory brainstem response. We also examine lateralized immunocytochemical changes in midbrain following one-sided trauma. With a better understanding of the mechanism involved in the generation of tinnitus, we will use this model to understand the mechanism of action of Lidocaine, the only drug known to consistently, albeit temporarily, provide relief.

Distinct temporal lobe projections to auditory and visual regions in the ventral prefrontal cortex support face and vocalization processing.

Maria M. Diehl, Jennifer A. Bartlow-Kang, Tadashi Sugihara, Lizabeth M. Romanski
Department of Neurobiology & Anatomy, University of Rochester, Rochester, NY

The integration of face and voice information is required for communication in human and non-human primates. Electrophysiological recording studies in ventrolateral prefrontal cortex (VLPFC) have examined responses to complex auditory, visual, and multisensory stimuli. Neurons responsive to complex auditory stimuli including vocalizations have been localized to anterior VLPFC, within a discrete region of area 12/47, whereas responses to complex visual stimuli, including faces, can be evoked over a larger part of VLPFC that includes portions of lateral area 12/47, lateral orbital cortex, and area 45. Furthermore, when face and vocalization stimuli are presented simultaneously, multisensory, audiovisual responses can be elicited from some VLPFC neurons within these same regions. We recorded auditory, visual, and multisensory responsive neurons from VLPFC and using these physiologically-defined boundaries, placed anatomical tracers into distinct locations to determine the afferent and efferent projections of the auditory and visual responsive cells. Our results demonstrate that prefrontal auditory neurons receive the densest input from superior temporal gyrus (STG) areas TAa, the anterior parabelt, and to a lesser extent TPO. In contrast, visually responsive neurons in VLPFC receive afferent projections from a number of inferotemporal cortex areas including TE, IPa, PGA and TPO. Injections placed in the inferior convexity between the auditory and visual selective regions, where neurons responded to both auditory and visual stimuli received inputs mainly from TPO and to a lesser degree areas TAa, IPa and TE. Finally, all of our injections resulted in retrograde labeling of the amygdala and anterograde labeling of the striatum. By investigating the anatomical connections of the VLPFC, we hope to better understand how auditory and visual information reaches the frontal lobes. The information gained from our tracing studies may provide clues as to the neural circuit that underlies integration and processing of communication information.

Adaptive, state-dependent acquisition and extinction of auditory and visual target responses in the ferret prefrontal cortex

Jonathan Fritz, Stephen David, Pingbo Yin, Shihab Shamma
Neural Systems Lab, Inst. Syst Res., Univ. Maryland, College Park, MD

One of the defining features of neurons in the primate prefrontal cortex (PFC) is selective encoding of task-relevant information. How is salient information identified and acquired by PFC and modified during changing behavioral task conditions? What are the responses of PFC neurons in non-task

states to previously relevant stimuli? Guided by a recent neuroanatomical study (Duque et al., 2008) that mapped out ferret prefrontal cortex (PFC), we initiated neurophysiological studies in the PFC of behaving ferrets. They were trained on multiple auditory detection and discrimination tasks, and a simple visual discrimination task, using conditioned avoidance techniques. We recorded neuronal responses (n=620) to acoustic and visual stimuli in dorsal PFC (dorsal orbital gyrus and anterior sigmoidal cortex) of three head-fixed ferrets during quiescent (non-task) states and also while the animals were performing a sequence of multiple tasks. We observed responses in ferret dorsal PFC that were similar to those reported in earlier studies in the monkey, being highly adaptive, selective, and categorical. During behavior, we observed rapid learning of task-relevant information, manifested in a variety of selective target recognition responses that categorically distinguished between novel target and distractor stimuli, ranging from phasic responses (75-150 ms latency after target onset), to sustained responses that lasted throughout the target stimulus (>1 sec) until the animal's behavioral response. We compared target responses in the same PFC neurons during multiple successive task conditions. Responses to targets were often independent of the sensory properties or modality of the targets in multiple tasks and thus could encode behavioral "meaning" - an abstract representation of a broad class of task-relevant stimuli, which was linked to a specific behavioral response (inhibition of licking). We also found that responses to target stimuli initially persisted in post-behavioral testing in a quiescent "non-task" condition but then gradually extinguished with a variable half-life of ~5-100 minutes. Our results suggest that the PFC rapidly resets responses in a state-dependent manner, tracking task-relevant information in changing task conditions. However, in passive non-task conditions, responses to incoming information may be shaped by a fading memory of the behaviorally relevant target from the most recent task. In sum, these findings suggest that the ferret PFC may provide an exciting new model system to study the cognitive control of behavior and the time-course and nature of encoding of task-relevant information in PFC.

Since the time course of acquisition and extinction of target representations in PFC paralleled the trajectory for task-related receptive field plasticity in A1, primary auditory cortex (Fritz et al., 2003, 2007), we have also begun simultaneous recording in PFC and A1. Preliminary results support the possibility that PFC may contribute to top-down modulation of A1 responses. Thus PFC neurons adaptively code information that is most salient for current behavior.

Network Precision Plasticity for Communication Calls in Awake Mouse Auditory Cortex

Edgar Galindo-Leon and Robert C. Liu

Department of Biology, Emory University, 1510 Clifton Road NE, Atlanta, GA 30322

Center for Behavioral Neuroscience, Atlanta, GA 30302

There is a growing interest in how the local field potential (LFP) encodes stimulus parameters. Few studies though have investigated the stimulus-evoked LFP's intrinsic variability, which ultimately limits its information encoding. We recorded LFP's along with single units (SU) to investigate this in the context of species-specific communication processing, studied for the first time in the awake mouse auditory cortex. We played back natural ultrasonic (~60-80 kHz) vocalizations emitted by mouse pups to awake, head-restrained female mice that either do (mothers) or do not (virgins) recognize the behavioral relevance of these calls. We viewed the evoked LFP response as transient, relatively depolarizing and hyperpolarizing events, and studied the variability in their timing and amplitude. We discovered that the precision in the timing of evoked LFP events increased significantly faster and earlier in mothers compared to virgins, even though the overall mean LFP was similar between groups. This plasticity in the trial-by-trial call-evoked LFP precision produced a more globally synchronized feed-forward network response across the awake auditory cortex, potentially facilitating improved call information processing. Combined with changes in single unit responsiveness, this work presents new evidence for distributed cortical network plasticity for communication sound processing.

Investigation of cortical pitch processing in humans using depth electrode recording

T. D. Griffiths¹, S. Kumar¹, W. Sedley¹, K. Nourski², H. Kawasaki², H. Oya², J. F. Brugge², M. A. Howard²;

¹Auditory Group, Newcastle Univ., Newcastle upon Tyne, United Kingdom; ²Univ. of Iowa, Iowa City, IA

Pitch is a perceptual attribute of sound that forms a basis for melody in music and prosody in speech. Neurophysiological recordings in monkeys (Wang et al, 2005) have been interpreted in terms of a pitch center close to the border of primary and secondary areas whilst human work using fMRI and MEG (Patterson et al, 2002; Penagos et al 2004; Krumbholz et al 2003) indicates specialized mechanisms in secondary areas in lateral Heschl's Gyrus (HG) for processing pitch. In this study we examined electrical activity in humans in primary and secondary areas of HG corresponding to the transition from control noise to a regular-interval-noise (iterated rippled noise, IRN). Our aim was to show electrical responses in lateral HG that might correspond to a neural correlate of the percept of pitch, instead of encoding the stimulus structure.

The stimulus was a 1-s noise immediately followed by 1.5-s of IRN. The number of iterations, and corresponding pitch strength, was increased from 0 to 32 in six equal log steps with a fixed pitch of 128 Hz. The stimulus was high-pass filtered at 800 Hz to minimise the resolvable spectral changes. Intracranial recordings were obtained from three neurosurgical patients from 14 high impedance depth electrodes, where the electrode placement was along the axis of HG so as to allow simultaneous recording from primary and secondary areas. Analyses were carried out to determine average evoked potentials (AEPs) and induced time-frequency responses at each.

AEP peak height for noise onset was maximum in the primary area within postero-medial HG. AEP peak height for IRN onset was monotonically related to the number of iterations in all the electrodes in primary areas in postero-medial HG, extending to secondary areas in middle and lateral portions of HG. The maximum AEP magnitude in response to IRN onset was in secondary cortex in the middle part of HG. Induced responses were maximal 300 ms after the noise-pitch transition in the 80-120 Hz frequency range, and power in this range was also monotonically related to the number of iterations. Induced responses occurred in primary areas in posteromedial HG and extended more laterally than the evoked potential response to the most lateral part of HG.

The induced electrical responses extend to lateral regions of HG that are maximally activated in previous work that mapped the fMRI BOLD response. An interpretation consistent with the data is that these responses are both neural correlates of the pitch percept.

References

- Bendor *et al* (2005) *Nature*, 436, 1161-1165
Krumbholz *et al* (2003) *Cereb Cortex*, 13, 765-772
Patterson *et al* (2002). *Neuron*, 36,767-776
Penagos *et al* (2004). *J Neurosci*, 24, 6810-6815

Human psychophysics of spectral and temporal modulations and their interaction: a systematic approach to the processing of dynamic ripples.

Manon Grube, Paul Eastaugh, Timothy D Griffiths.

Med. Sch., Newcastle Univ., Newcastle upon Tyne, United Kingdom

This study assesses spectral, temporal and dynamic (spectro-temporal) modulation processing in the human brain. Spectro-temporal modulations are ethologically valid stimuli used for behavioral and neural responses in animals [1-4] and humans before [5-6].

The present battery systematically tests detection and discrimination of purely spectral and temporal modulations, dynamic modulation detection, dynamic spectral and temporal discrimination, and difference ratings for dynamic modulations. Stimuli (100 components/octave; .25-4 kHz) have sinusoidal amplitude modulations of the frequency spectrum (density; .5-1.5 cycles/ octave) and over time (velocity; 4-16 cycles/ second). Detection and discrimination tests are based on adaptive (2 down 1 up) procedures estimating 71% correct thresholds (for 2 rates with 50 trials each). Tests were run on 20 naïve subjects (30-79 years; 8 males).

The data allow a conclusive inference of spectral-temporal modulation processing based on correlation analysis (significance level, $p < .05$). Within tasks, thresholds were correlated between rates (densities or velocities), supporting tapping into the same process. Detection and discrimination of the same type of modulation were not correlated, suggesting that differentiation of rates depends not only

on modulation sensitivity. No correlations were found between detection tests, implicating different (lower-level) mechanisms. Discrimination tests were in part correlated: purely temporal and dynamic velocity were correlated, purely spectral and dynamic density were not, but dynamic velocity and density were, indicating that temporal and dynamic processing share a common neural basis. Purely spectral and temporal discrimination were not correlated.

The findings are consistent with the existence and interaction of separable brain mechanisms for the processing of spectral, temporal and dynamic modulations that are typical of natural auditory events. The robustness of results encourages the use of these tests in assessing spectro-temporal processing in the disordered brain.

References

- 1 Kowalski, N., Depireux, D.A., Shamma, S.A. (1996). *J Neurophysiol* 76.
- 2 Depireux, D.A., Simon, J.Z., Klein, D.J., Shamma, S.A. (2001). *J Neurophysiol* 85.
- 4 Linden, J.F., Liu, R.C., Sahani, M., Schreiner, C.E., Merzenich, M.M. (2003). *Journal Neurophysiol* 90.
- 3 Woolley, S.M., Fremouw, T.E., Hsu, A., Theunissen, F.E. (2005). *Nat Neurosci* 8.
- 5 Chi, T., Gao, Y., Guyton, M.C., Ru, P., Shamma, S. (1999). *J Acoust Soc Am* 106.
- 6 Langers, D.R., Backes, W.H., van Dijk, P. (2003). *Neuroimage* 20.

Stimulus specific adaptations in the gaze control system of the barn owl (*Tyto alba*)

Yoram Gutfreund and Amit Reches

Department of Physiology and Biophysics, The Ruth and Bruce Faculty of Medicine, Technion, Haifa 31096, Israel

Gaze control circuitry is believed to be intimately linked with the control of spatial attention to salient stimuli. We therefore characterized a neurocorrelate of novelty detection, stimulus-specific adaptation (SSA), in gaze control centers in the forebrain and midbrain of the barn owl. We have found SSA to be highly ubiquitous. Neurons tended to respond stronger to rare sound features such as frequencies, interaural time differences, interaural level differences and sound intensity. In addition we report that neurons in the same centers tended to respond stronger to rare visual features such as movement direction and spatial location. Finally we examined SSA in bimodal scenes and show that the novelty response is enhanced when a rare visual is presented synchronously with a rare auditory stimulus. The manifestation of SSA in such a variety of independent acoustic and visual features, in both the forebrain and the midbrain, supports the notion that SSA is involved in sensory memory and novelty detection.

VGLuT2 Expression in the Auditory Cortex of Primates

Troy A. Hackett, *Vanderbilt University School of Medicine, Dept. of Hearing and Speech Sciences*

Lisa A. de la Mothe, *Vanderbilt University, Dept. of Psychology*

The auditory cortex of primates receives thalamic inputs from four subdivisions of the medial geniculate complex (MGC), but the cortical targets of each division vary. Notably, the ventral division (MGv) projects mainly to areas within the core region, while the posterodorsal division (MGpd) projects to most of the belt and parabelt areas. The projections terminate in layer IV and lower layer III and are assumed to be glutamatergic. Vesicular glutamate transporters (VGLuT) regulate glutamate stores in synaptic vesicles. In cortex, the VGLuT2 isoform is concentrated in thalamocortical terminals. In the present study, VGLuT2 immunohistochemistry was used to index the glutamatergic projection across regions of auditory cortex. Series of coronal sections from the macaque monkey were processed to reveal VGLuT2 and other markers concentrated in the layer III/IV band including cytochrome oxidase (CO), acetylcholinesterase (AChE), and parvalbumin (PV). Expression of each marker was studied with wide field and confocal microscopy. The main findings were: 1) VGLuT2 expression was primarily focused in the neuropil of the layer III/IV band; 2) VGLuT2 expression was coextensive with elevated expression of PV, AChE and CO; 3) VGLuT2 expression was highest in the core areas, intermediate in the belt, areas and weakest in the parabelt; 5) VGLuT2+ terminals were colocalized on some somata ,

but were concentrated in the neuropil between cells. The results indicate that the glutamatergic thalamic input diminishes in magnitude along the core-belt-parabelt axis, suggesting that the functional impact of the thalamic projection may decrease along the core-belt-parabelt processing hierarchy. The results also reveal differences in the functional contributions of the MGv and MGpd to auditory cortical processing.

Parallel electrophysiological and behavioral analysis of layer-specific electrical microstimulation in primary auditory cortex - implications for the subcortical loop hypothesis

M.F.K. Happel^{1,2}, M. Jeschke¹, J. Handschuh^{1,2}, M. Deliano¹, F.W. Ohl^{1,2}

1BioFuture Research Group, Leibniz Institute for Neurobiology, Magdeburg, Germany; 2Inst. for Biol., Otto-v.-Guericke University, Magdeburg, Germany

For developing sensory cortical neuroprostheses it is important to determine the generators of electrically evoked cortical responses and their neuronal dynamics. One obstacle for a detailed understanding of how intracortical microstimulation (ICMS) interfaces with cortical processing is that the roles and forms of intracortically (IC) and thalamocortically (TC) evoked neuronal activities, as well as the role of corticothalamic (CT) backpropagating feedback loops in particular, are not well known [1]. Behavioral studies revealed that infragranular stimulation has the lowest threshold [2] that could in principle be due to activation of subcortical loops. The objective of this study was a parallel electrophysiological and behavioral analysis of layer-specific ICMS in primary auditory cortex AI of the Mongolian gerbil. We used current source density (CSD) analysis to compare acoustical stimulation and ICMS. Electrically evoked and acoustically evoked CSD profiles were similar in terms of spatiotemporal arrangement of current sources and sinks suggesting the recruitment of similar neuronal elements. Then, intracortical sources of activity were suppressed by topical application of GABA_A-agonist Muscimol to disentangle TC and IC contributions to the CSD profiles [3]. During the pharmacological blockade a layer IV-sink, corresponding to the lemniscal TC input, was still visible with acoustical but not with electrical stimulation. The fact that this is true even for strong infragranular stimulation indicates principal relevance of intracortical connections for ICMS-evoked profiles. In order to exploit the neuronal dynamics evoked by ICMS for neuroprosthetic applications we determined the laminar threshold variation in a behavioral ICMS detection task using a shuttle-box paradigm. Analysis of psychometric functions revealed that ICMS in the granular and infragranular layers (IV-VI) yielded lower behavioral thresholds compared to ICMS in supragranular layers. We found biphasic bipolar stimulation to be more reliable and efficient than biphasic monopolar stimulation. Further implications of the combined electrophysiological and behavioral results for the role of subcortical loops in ICMS-evoked perception will be discussed.

References

[1] DeYoe et al, J Neurophys (2005)

[2] Tehovnik et al, J Neurophys (2005)

[3] Kaur et al, J Neurophys (2004)

Supported by: NIDCD DC03180 (XW) and DC06357 (ELB) and the Deafness Research Foundation (ELB)

Long-Term Tracking of Spectro-Temporal Receptive Fields

Drew Battenfield Headley and Norman M. Weinberger,

UC Irvine

Spectrotemporal receptive fields (STRFs) are increasingly used to describe auditory tuning in behaving animals. Using STRFs benefits studies of associative plasticity in the auditory system since they can be rapidly obtained during training and without extinguishing behavioral responses to conditional stimuli (pure tones). However, it has not been evaluated whether STRFs are stable over the minutes and weeks necessary to track long-term associative plasticity.

Prior to using STRFs during a training task we needed to determine their intrinsic variability on time scales reflecting rapid induction and long-term retention. Towards this end, we chronically

implanted microwire arrays into the primary auditory cortex of rats. Multiple unit recordings were made while both ripple and pure tone stimuli were presented. Ripples were moving sinusoidal logarithmic frequency gratings with spectral modulations up to 1.4 cycles/octave and temporal modulations not exceeding 20 Hz. Ripple intensities varied between 40-60 dB, while pure tones were from 10-70 dB.

We found that over a period of tens of minutes the signal to noise for an STRF generated by a single repetition of ripple stimuli can vary. However, a STRF's best frequency can remain stable over minutes and weeks. In most cases the STRF and frequency receptive fields gave the same best frequency. This work sets the stage for the integration of STRFs into the study of associative memory.

The effect of global and attentional state on forward masking in rat auditory cortex

L. Hollender¹, G. H. Otazu², A. Renart¹, L.-H. Tai^{2,3}, K. D. Harris^{1,4};

¹*Ctr. Mol & Beh Neurosci, Rutgers Univ., Newark, NJ*; ²*Cold Spring Harbor Lab., Cold Spring Harbor, NY*; ³*Grad. Program in Neurosci., Stony Brook University, NY*; ⁴*Smilow Neurosci. Program and Dept. of Otolaryngology, New York Univ. Sch. of medicine, New York, NY*

The ability of animals to discriminate stimuli depends not only on the structure of the stimuli, but also on the state of the animal's brain. Here we investigate how neural processing of acoustic stimuli of fast temporal structure varies with brain state, using population recordings in the auditory cortex of urethane-anesthetized and awake rats.

The state of the cortex varies between a "synchronized" state (up-down oscillations), typical of quiet wakefulness or slow-wave sleep, and a "desynchronized" state typical of alert wakefulness or REM. To assess how the processing of temporally structured sounds varies with cortical state, we used a two-click paradigm. 5ms clicks were presented either individually, or in pairs with a 50ms inter stimulus-interval (ISI). Such short ISIs are known to evoke a decreased cortical response ('Forward Masking'). We hypothesized that the ability of auditory cortical spiking to predict which stimulus had been presented would be greater in the desynchronized state.

In urethane anesthetized rats, we found that the global state of the brain significantly modulates the quality of the stimulus representation by neuronal populations. Using classification techniques we found that different stimuli presented in the desynchronized state did indeed evoke more discriminable firing patterns than stimuli presented in the inactivated state. In both states, the response to the second click was suppressed compared to the first, as previously described for the forward masking paradigm. However, the improved discriminability in the desynchronized state did not result from a reduction in this suppression. Rather, it resulted from differences in response variability and correlation and response time-scale between the two trial types. In the activated state, single and double click trials evoked distinct activity patterns, and trial-to-trial variability was low. In the inactivated state, however, trial-to-trial variability was greater, and also correlated amongst simultaneously recorded neurons, resulting in poor discrimination performance.

To investigate whether similar effects might occur in unanesthetized animals, we analyzed data from rats either performing an auditory discrimination task, or passively listening. Even though firing rates were significantly higher in the inattentive condition, response variability was lower when the rat was engaged in the task. We conclude that cortical activation and attention results in improved representation of complex auditory stimuli not by increasing firing rates, but by lowering response variability.

Encoding of correct and incorrect responses by ventral prefrontal cortex neurons in an audiovisual discrimination task.

Jaewon Hwang¹, Mark D. Diltz², and Lizabeth M. Romanski²

¹*Brain & Cognitive Sciences*, ² *Department of Neurobiology & Anatomy, University of Rochester, Rochester, NY*

Previously we recorded the activity of single neurons in the primate ventrolateral prefrontal cortex (VLPFC) with an audiovisual discrimination (non-match-to-sample) task in which face-vocalization movie clips were used as stimuli. During the task, monkeys attended the audiovisual stimuli and were

required to press a button when a non-matching stimulus, i.e. one whose auditory or visual track differed from the sample movie, occurred. In our task, the non-match would appear as either the first or the second audiovisual stimulus after the sample. The subjects detected the non-match by pressing a single response button in order to receive a juice reward. Our analyses have shown that some cells in VLPFC are sensitive to task demands while others may encode stimulus properties. In order to better understand how prefrontal neurons participate in the discrimination of audio-visual communication signals we have analyzed neuronal activity during several instances of correct and incorrect trials during audio-visual discrimination. We compared activity when subjects correctly detected a non-match stimulus and when they failed to respond to that same non-matching stimulus. 13% of neurons showed significantly different activity during the non-match period in correct responses compared to failures to respond. In addition, we examined neural activity when subjects correctly detected a non-match and when they incorrectly responded to a matching stimulus. We hypothesized that if subjects have learned to withhold responding when the stimulus presented matches the sample, then activity during match presentation may differ when they correctly withhold a response and when they do not. In 12% of neurons, activity between those two cases was significantly different. Furthermore, we found that these populations of cells encoding correct and incorrect discrimination trials were not sensitive to stimulus properties in the sample and non-match period. Only a small proportion of error encoding cells had activity related to the sample audiovisual stimulus or the non-match audiovisual stimulus. Our results suggest that neurons in VLPFC are actively involved in the discrimination of audio-visual communication information and that VLPFC may play a role in translating audio-visual signals into decisions.

The effects of sleep on sound processing in auditory cortex

Elias B. Issa & Xiaoqin Wang

Laboratory of Auditory Neurophysiology, Department of Biomedical Engineering, Johns Hopkins University

Typically, sleep is considered an internal state, shut off from the external world and influenced by endogenous brain rhythms. This perspective, where low frequency oscillations organize activity, has helped in understanding the dynamic behavior of neurons during sleep. Here, we took a different approach and studied the sleeping brain under the influence of external stimulation. This approach is interesting in its own right since many have been curious as to why most sounds do not reach perception during sleep while some, such as our own name, can easily awaken us. Using sounds, we were able to elicit activity in the auditory cortex of naturally sleeping marmosets. Recording from single neurons, pairs of neurons, and the local field potential, we report the following findings in slow-wave sleep: strong activity in response to loud sounds even in secondary auditory areas, a loss, however, of responses to quiet sounds and the dynamic range of responses, and enhanced correlated activity. Interestingly, these properties did not change as dramatically in dream sleep, which was more similar to wakefulness. Our observations in slow-wave sleep could not be explained strictly by the presence of slow oscillations since some effects were specific to periods of acoustic stimulation. Instead, a simple model utilizing reduced inhibition replicated a wide range of our observations. These initial findings illustrate a complicated interplay between sleep networks and sounds and have novel implications for how hearing changes during sleep.

Compartmental analysis of sound-induced Arc/Arg 3.1 mRNA expression in mouse auditory cortex

Tamara Ivanova*, Christina Gross**, Gary J. Bassell**, Robert C. Liu*

**Emory University, Dept Biology, **Dept of Cell Biology and Neurology, Atlanta, GA 30322*

In previous studies in a mouse model, we found a long term plasticity in the auditory cortical response to species-specific communication sounds which correlated with their behavioral relevance (Liu et al, 2006, 2007). To investigate the cell and molecular mechanisms underlying this electrophysiological change, we have begun exploring the expression of activity-dependent effector immediate early genes

with known roles in synaptic plasticity. Of particular interest is the cytoskeleton-associated gene Arc/Arg 3.1, which has been strongly implicated in memory consolidation and function (Tzingounis and Nicoll, 2006). Our first step has been to investigate the expression of Arc/Arg 3.1 mRNA (EAAR) in the mouse auditory cortex in response to sound stimulation. Female mice (18-19 weeks old CBA/CaJ) were housed in silence in an anechoic chamber for 4 h before a 10-min period of sound stimulation by a dynamically modulated 32 kHz tone. Mice were then left in silence again for either 0, 30 or 60 minutes before decapitation. Mice in the control group were housed in the chamber in silence for 5 h 10 min. EAAR in auditory neuronal cells was analyzed by cellular compartmental analysis of fluorescence in-situ hybridization (FISH) of serial coronal sections (20 μ M). Nuclei were identified by DAPI staining. Images were collected using a Zeiss laser scanning confocal microscope.

Sound stimulation led to temporally differentiated increases in auditory cortical EAAR within the nucleus and cytoplasm. After the end of sound stimulation, intense intranuclear foci of Arc/Arg 3.1 appeared immediately in nuclei of middle layer cells. EAAR was detected only in the cytoplasm and dendrites of all cortical layers 30-60 min after the end of the stimulation. Sound stimulation did not evoke any changes in the EAAR in the visual cortex. Our results demonstrate that Arc/Arg 3.1 mRNA expression and dendritic localization in the auditory cortex can be driven by acoustic stimulation, where the initial nuclear expression is targeted into the cytoplasm and dendrites within 30 minutes. Hence, this data provides a time course for cellular compartmental Arc/Arg 3.1 expression, which can next be used for more complex temporal acoustic stimulation paradigms. Acknowledgements: Research partly funded by NIH grants DC008343 (RCL) and NS051127 (GJB).

Role of auditory cortex in auditory attention in time

Santiago Jaramillo, Allison E. Baker & Anthony M. Zador
Cold Spring Harbor Laboratory

When a stimulus occurs at a predictable instant in time, anticipation of the stimulus improves the speed and accuracy with which it is detected. This phenomenon is sometimes referred to as "temporal orienting" or "attention in time".

We have developed a two-alternative choice task paradigm in freely moving rats to study the neural mechanisms underlying auditory attention in time. We find that: (1) temporal orienting improves reaction time and performance; (2) the auditory cortex is necessary for the task; (3) neuronal activity in the primary auditory cortex is modulated by temporal expectation.

We first trained rats to detect a frequency modulated sound immersed in a train of pure tones. Animals were rewarded for correctly responding to the central frequency of the modulated target in a given trial. Behavioral analysis showed a clear improvement in reaction times whenever the target appeared at an expected moment, compared to the same target appearing unexpectedly. We next used the GABA-A receptor agonist muscimol to inactivate reversibly the auditory cortex. Muscimol inactivation dramatically impaired performance compared with control application of saline, implying that the auditory cortex is essential for this task. Finally, we used tetrodes to record responses from single neurons in the primary auditory cortex of rats performing this task. Responsive neurons often showed an increase evoked response to tones immediately preceding the expected location of the target when compared against responses to the same tones occurring long before the expected target location. Our results represent a first step toward understanding how attention in time enhances stimulus processing in the auditory cortex.

Song recognition learning drives experience-dependent representations in the auditory forebrain region CLM

James Jeanne^{1,2,3}, Tatyana Sharpee^{1,2}, Timothy Gentner^{1,3}
1Neurosciences Grad. Program, Univ. of California, San Diego, La Jolla, CA; 2Salk Institute for Biological Studies, La Jolla, CA; 3Dept Psychol, Univ. California, San Diego, La Jolla, CA

The song-recognition system of oscine birds provides an excellent model for investigating the mechanisms that underlie the perception and cognition of complex, natural acoustic communication

signals. In European starlings (*Sturnus vulgaris*), song recognition learning can exert strong effects on the response properties of neurons in the caudomedial mesopallium (CMM), a region analogous to mammalian secondary auditory cortex. The CMM neurons respond more strongly to the songs that birds have learned to recognize than to unfamiliar songs and are biased by differences in associative reinforcement during training. A subset of CMM neurons are selective for small numbers of the functional units (motifs) in single familiar songs. The neural circuitry that gives rise to this selectivity is not understood. Here we investigate the experience-dependent representation of natural songs in the caudolateral mesopallium (CLM), a forebrain auditory region immediately afferent to CMM with strong reciprocal connections to CMM and Field L, the analog to mammalian primary auditory cortex. We trained 5 starlings on a go/no-go operant song recognition task, anesthetized them with urethane, and recorded responses of single neurons (N=44) in CLM to training and unfamiliar songs. We find the responses of neurons in CLM are biased by the behavioral experience of each bird, but less so than in CMM. Like the neurons in CMM, those in CLM respond more strongly overall to the set of training songs than to a set of unfamiliar songs. However, there are fewer song-selective neurons in CLM than there are in CMM, and those that are selective are not biased significantly towards the training songs. Moreover, differences in associative pairings between reinforcement and specific training songs do not appear to affect CLM responses as they do in CMM. This pattern of results is consistent with a hierarchical model for experience-dependent song selectivity in which the effects of reinforcement and the emergence of responses tied to task-specific diagnostic stimulus components occurs within the caudal mesopallium, but subsequent to CLM. To investigate this emerging selectivity, we are modeling single-unit responses across CM. Single-feature Linear Nonlinear (LN) models explain, on average, 12.1% (range 2%-50%) of the information in the neural response of CLM cells and 10.8% (range 1%-38%) of the information in the neural response of CMM cells. This suggests that responses of neurons in CM are based on multiple stimulus features, an idea which we are actively pursuing.

Effect of training paradigms on behavioral strategy in an auditory discrimination task

M. Jeschke¹, F. W. Ohl^{1,2};

¹*BioFuture Res. Group, Leibniz Inst. for Neurobiology, Magdeburg, Germany*

²*Inst. for Biol., Otto-von-Guericke Univ. Magdeburg, Magdeburg, Germany*

Numerous studies have demonstrated that the performance in a behavioral discrimination task is linked with the number of items to be discriminated. We wondered whether this could be an effect of training paradigms. It might well be that "additive" training procedures in which the complexity of a task is increased in a stepwise fashion – e.g. as in response shaping – might result in superior performance by enabling subjects to filter out relevant aspects of the task while ignoring others. Our aims were two-fold: 1) to test whether our experimental animals (Mongolian gerbils, *Meriones unguiculatus*) are able to discriminate 1 target sound from 3 non-target sounds and 2) to investigate the effect of different training paradigms on this type of auditory discrimination learning.

Two groups of gerbils were trained to discriminate four frequency modulated sweeps (FMs) in a GO/(NO-GO) two-compartment shuttle-box task to avoid a mild electric foot-shock. Group 1 had to discriminate all four FMs from the beginning of the training while group 2 was initially trained to discriminate two FMs and after nine training sessions the other two FMs were introduced.

We found that animals performed significantly better and learned faster if initially trained with two rather than four stimuli. Qualitatively, adding two more stimuli during the training resulted in intermediate learning speed and accuracy. Interestingly, during the second phase animals in group 2 showed a specific pattern of errors. FMs that traversed the same frequency range as the target, but with opposite modulation direction, were confused significantly more often than stimuli with the same frequency range as the original non-target. No such bias was found for group 1 animals. Therefore, our results provide clear evidence that gerbils in group 2 use the frequency range of the stimuli to solve the task. In conclusion, our data show that the same general training paradigm including the exact same stimulus set can lead to very different learning strategies based on the temporal structure of the training paradigm.

The contribution of different neural codes to the encoding of natural sounds in auditory cortex

Christoph Kayser¹, Marcelo A. Montemurro², Nikos K. Logothetis¹, Stefano Panzeri^{2,3}

¹ *Max Planck Institute for Biological Cybernetics, Spemannstrasse 38, 72076 Tübingen, Germany*

² *Faculty of Life Sciences, University of Manchester, Manchester M60 1QD, United Kingdom*

³ *Robotics, Brain and Cognitive Sciences Department, Italian Institute of Technology, Via Morego 30, 16163 Genova, Italy*

How neurons encode sensory information is still matter of debate. While some argue for firing rates as neural code, others emphasize temporal properties, such as spike-patterns or the relation of spikes to ongoing network fluctuations. Using the primate auditory cortex as a model system, we determined the relative contribution of such temporal codes to the encoding of natural sounds. Overall, the temporal codes provided much more information than firing rates. The phase of spike times with respect to slow field potentials (tens-millisecond scale) was the biggest source of temporal information and was the most robust to sensory noise. However, stimulus-clocked spike patterns (few-millisecond scale) provided additional information not available from spike rates or spike phases alone. Combining different coding strategies hence offers a computational advantage over using a single code alone. Extending this analysis to a cross-modal paradigm demonstrates that the influence of visual stimuli on caudal auditory regions manifests more in temporal codes while firing rates are only little affected. Overall our results show that sensory cortices could rely on the concurrent use of several nested time scales to encode information, each of which might provide complementary evidence about the natural environment.

Caudorostral progression of auditory information processing on the monkey's supratemporal plane

*Y. Kikuchi^{1,2,3}, B. Horwitz², M. Mishkin³;

¹*Physiol & Biophysics, Georgetown Univ. Med., Washington, DC;* ²*NIDCD, Bethesda, MD;* ³*NIMH, Bethesda, MD*

Anatomical evidence suggests that the auditory core constitutes the first stage of auditory cortical processing, with a serial progression from core outward, first to the surrounding auditory belt and then to the parabelt. The connectational evidence also suggests that the core itself (AI, R, and RT) is serially organized with a stepwise progression from A1 through R and RT to even more rostral parts of the supratemporal plane (STPr). We hypothesized that the STPr contains the anterior extension of a rostrally directed auditory pathway, and, in particular, that auditory subdivisions within the STPr form the continuation of a stimulus-quality processing stream originating in the auditory core area A1. Here we analyzed single-unit activity, multi-unit activity, and local field potentials (LFP) distributed caudorostrally along the STP in: (i) caudal STP, including mainly A1; (ii) the middle part of STP (STPm); and (iii) the rostral part of STP (STPr), including cortex located within 3 mm of the tip of the temporal lobe. During recording sessions the animals performed an auditory task in which they discriminated between a positive stimulus (white noise) and any of 40 negative stimuli – 20 monkey vocalizations and 20 other sounds – which were the stimuli of interest. At the cellular level, the mean onset latency of auditory excitatory responses increased progressively from loci i to iii, while the mean number of stimuli that were effective for individual cells decreased progressively. The greatest concentration of cells for which a monkey call was the best stimulus (i.e. evoked the highest discharge rate) was located in the medial portion of STPr, including the lateral bank of the circular sulcus. At the population level, significant auditory-evoked LFPs were observed in all three auditory loci. The LFPs in loci ii and iii also showed significant, though broadly tuned, stimulus selectivity. The results suggest that the STP contains a rostrally directed, hierarchically organized auditory processing stream, with gradually increasing stimulus selectivity, and that this stream extends from the primary auditory area to the superior temporal pole. *Support: Intramural Research Programs of NIMH and NIDCD*

Manipulation of Neuronal Responses with Activity-Triggered Microstimulation

Woosung Kim, Dennis L. Barbour

Biomed. Engin., Washington Univ., St.Louis, MO

Department of Biomedical Engineering, Washington University, St. Louis, MO, USA

Cerebral cortical neurons can change their response properties under natural conditions that induce rapid neural plasticity such as peripheral injury. Similar rapid changes can also be induced under artificial conditions such as pharmacologic manipulation, presumably by altering synaptic weights across the neural network. In order to induce targeted, functional reorganization of primary auditory cortex (A1) neurons by manipulating synaptic weights directly, we adopted a method of triggered microstimulation to strengthen the synaptic weights between two distant sites within A1. In this paradigm, neuronal activity in one portion of A1 was used to trigger delivery of microstimulation current pulses to an electrode located in another portion of A1 tuned to a different sound frequency. Following several hours of this artificially-induced activity correlation, retesting the neuronal responses often revealed physiological alteration of sound frequency response at the stimulated site such that the stimulated region more closely matched the frequency tuning of the recorded region. Frequency tuning of the recorded site generally remained unchanged. This targeted functional cortical remapping technique can therefore rewire neuronal circuits in the adult neocortex and may ultimately prove useful for bypassing damaged brain areas and recreating a particular brain function in remote areas of the adult brain.

The auditory association cortex required for discrimination learning of synthetic speech sounds in rats

M Kudoh¹, R Hishida², K Shibuki²

1Dept Physiol, Teikyo Univ Sch Med, Tokyo, 173-8605, Japan, 2Dept Neurophysiol, Brain Res Inst, Niigata Univ, Niigata, 951-8585, Japan

We have reported that discrimination learning of synthetic vowel-like sounds with multiple formants requires the presence of the rostral/dorsal auditory association cortex in rats. In the present study, characteristics of the synthetic vowel discrimination were investigated. Male Wistar rats deprived of water were trained to discriminate between two synthetic vowels. Licking a spout during presentation of one (S+) was rewarded with water while the other (S-) was not. Either S+ or S- was presented randomly in a trial, which was repeated every minute throughout a test session of 12 h on consecutive 4 days. Percentage of trials in which rats licked the spout was calculated separately for S+ and S-, and test performance was estimated as the difference. Discrimination of vowel-like sounds was examined at various formant frequencies. Rats could discriminate between two-formant sounds the frequency differences of which were comparable with those of F1 or F2 for human vowels, indicating that two-formant discrimination in rats can be regarded as an animal model of vowel discrimination in humans. We also investigated discrimination of voiced stop consonants /b, d, g/ characterized by transition of formants. Bilateral electrolytic lesions of the AC impaired discrimination learning of stop consonants with multiple formants, while discrimination between sounds with a single formant transition was not affected. Bilateral partial lesions of the rostral/dorsal, ventral or caudal auditory field attenuated discrimination learning of stop consonants. These findings suggest that discrimination learning of stop consonants requires activation of multiple auditory association fields in rats.

The effect of learning on vPFC auditory activity during a categorization task

Jung Hoon Lee, Lauren E. Orr, Brian E. Russ, Yale E. Cohen

Dartmouth College

Since the prefrontal cortex (PFC) plays an important role in goal-directed behavior, it is reasonable to hypothesize that the PFC is involved in categorization, an important component of goal-directed behavior. This hypothesis can be tested by recording from neurons in ventrolateral prefrontal cortex (vPFC), a part of the PFC that is involved in auditory-object processing. Our group has previously confirmed this hypothesis (Russ et al., 2007) by having monkeys categorize the spoken words *bad* and *dad* as well as morphs of these words. In that study, following extensive behavioral training, we

found that vPFC activity reflected the monkeys' behavioral reports (i.e., same or different). The results demonstrated a link between neural activity in vPFC and monkeys' reported choices.

Here, we examined how experience affects the monkeys' behavior and how experience affects neural activity during an auditory-categorization task. To test these questions, we recorded from auditory neurons in the vPFC while monkeys categorized a new class of human spoken words (i.e., *pad*, *tad*, and morphed versions of these two prototypes) in a delayed match-to-category task. In the delayed match-to-category task, monkeys reported whether a test stimulus was the same or different from a previously presented set of reference stimuli. The monkeys indicated their behavioral choices by making a saccade to one of two visual targets. Unlike our previous study in which recording began after extensive experience with the reference and test stimuli, in the current study, we recorded vPFC activity on the first day that the monkeys were exposed to these new stimuli. We found that monkeys quickly were able to categorize the spoken word reliably, and their performance improved in the ensuing days. In parallel with these behavioral changes, neural activity in the vPFC also changed. We found that as the monkeys' behavior improved, neural activity that indexed the monkeys behavioral reports also improved. We also tested whether this neural activity reflects the choices of the monkeys, independent of the stimuli, or whether certain populations of neurons were tuned to specific stimuli (i.e., *bad/dad* versus *pad/tad*). This study is consistent with the hypothesis that the vPFC, and the PFC in general, is involved in mediating aspects of goal-directed auditory behavior such as decision making.

Predicting first spikes at the onset of natural calls in the awake mouse auditory cortex

Frank G. Lin¹, Edgar Galindo-Leon², Robert C. Liu²

¹*Interdisciplinary Bioengineering Graduate Program, Georgia Institute of Technology, Atlanta, GA 30332*

²*Department of Biology, Emory University, Atlanta, GA 30322*

Communication sounds vary in acoustic properties such as frequency, duration and amplitude modulation. How the cortex represents these features for behaviorally-relevant vocalizations is one of the central questions of auditory neural coding. In theory, if we fully understood this encoding, we would be able to predict the auditory neural spiking in response to these natural sounds.

Understanding the mechanisms driving the first call-evoked spikes may be particularly interesting, since varying calls can elicit systematic differences in the timing of first spikes. However, models that have investigated first spike latency often cannot be directly applied to natural calls, since they were designed only for sounds at a neuron's characteristic frequency (CF). To bridge this gap, we look at predicting the first spikes of auditory cortical neurons in an awake mouse presented with species-specific ultrasonic communication calls. These calls consist of only single frequency whistles with varying durations, limited frequency modulations and more complex amplitude modulations (Liu et al, 2003; Liu 2006). Their relatively simple acoustic structure makes them ideal for extending models of auditory spiking beyond simple tones. One such model by Neubauer and Heil (2007) predicts the latency to first spikes in the auditory nerve fiber based on the leaky integration, event formation, and temporal summation (LIEFTS) of the sound pressure at the CF. We extended the LIEFTS model by incorporating a factor that modified the amplitude envelope leaky integration based on latencies measured for different tonal frequencies. Preliminary data demonstrates that this can improve the first spike prediction for natural calls. Extensions of this work may allow us to further understand how features of our sensory environment affect the precise temporal coding of spikes in the cortex.

Support provided by an NSF IGERT fellowship (FGL), NIH R01 DC008343 (RCL) and the NSF Center for Behavioral Neuroscience (RCL).

Stimulus-specific adaptation occurs in neurons of the medial but not ventral auditory thalamus

Jennifer F. Linden^[1,2] and Lucy A. Anderson^[1,3]

^[1]*JUCL Ear Inst.*, ^[2]*Dept. of Neuroscience, Physiol. & Pharmacol., Univ. Col. London, London, United Kingdom*; ^[3]*Auditory Neurophysiol. Unit, Inst. of Neurosci. of Castilla y Leon, Univ. of Salamanca, Salamanca, Spain*

Neurons in the primary auditory cortex respond more strongly to a rarely presented "deviant" tone than to the same tone when it is common, or "standard" (Ulanovsky, Las and Nelken, 2003; Ulanovsky, Las, Farkas and Nelken, 2004). This phenomenon, called "stimulus-specific adaptation" (SSA), has been proposed as a possible single-neuron correlate of the mismatch negativity (MMN), a cortical evoked potential associated with stimulus novelty. Previous studies in cat have suggested that SSA is absent from single neurons in the auditory thalamus (Ulanovsky et al. 2003, Ulanovsky et al. 2004); however, these reports did not differentiate between the auditory thalamic subdivisions. To explore the possibility of thalamic SSA more completely, we recorded extracellularly from 30 single units and 22 multiunit clusters in the ventral, medial, and dorsal subdivisions of the mouse auditory thalamus, while presenting the anaesthetized animals with sequences of standard and deviant tones. As in the cat studies, standard and deviant tone frequencies were separated by no more than 0.5 octaves, and evoked similar responses in most neurons. Using stimulation rates of 1.25 - 2.5 stimuli/s, we found SSA in neurons in the medial subdivision of the mouse auditory thalamus, but not in the ventral subdivision. The median neuronal stimulus-specific adaptation index (defined as in Ulanovsky et al. 2003) was significantly greater than zero in the medial subdivision at all stimulation rates tested (sign-rank test, $p < 0.05$), but was not significantly different from zero in the ventral or dorsal subdivisions for any of the tested stimulation rates. A smaller sample from the dorsal subdivision ($N = 13$ dorsal, compared to 20 medial and 19 ventral) also showed no significant SSA. Our results indicate that SSA does occur in the auditory thalamus, but only in the medial subdivision. Together with related findings of SSA in neurons of the "belt" regions of the inferior colliculus (Perez-Gonzalez, Malmierca and Covey, 2005), the findings suggest that SSA is either a general property of some neurons in the non-lemniscal auditory system, or a cortical phenomenon that influences subcortical auditory processing only within the non-lemniscal pathway.

Supported by: Gatsby Charitable Foundation Grants GAT2579/GAT2623, Deafness Research UK Grant 412:UEI:JL.

Contributions of specific auditory cortical areas to the enhanced visual abilities of the deaf

Stephen G. Lomber¹, M. Alex Meredith² and Andrej Kral³

¹*Departments of Physiology and Pharmacology, and Psychology, University of Western Ontario, London, ON, Canada;* ²*Department of Anatomy and Neurobiology, Virginia Commonwealth University, Richmond, VA, USA;* ³*Department of Neurophysiology and Pathophysiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

In the absence of acoustic input, it has been proposed that "deaf" auditory cortex may be recruited to perform visual functions. To test this hypothesis we examined the visual capabilities of three adult congenitally deaf cats and three adult hearing cats on a battery of visual tasks. For tests of grating acuity, Vernier acuity, direction of motion discrimination, velocity discrimination, and orientation discrimination performance of the deaf cats was similar to hearing cats. However, for two tests (movement detection and localization of a flashed stimulus) the deaf cats demonstrated enhanced performance. For deaf cats, movement detection thresholds were significantly lower than hearing cats. For the visual localization task, localization of peripheral positions was significantly better for the deaf cats. In the second part of the study we examined if cross-modal reorganization in auditory cortex may contribute to the enhanced visual capabilities of deaf cats. To accomplish this, we bilaterally placed cooling loops on A1, DZ, AAF, and PAF to permit their individual deactivation. Bilateral deactivation of PAF resulted in the elimination of the enhanced visual localization capabilities of the deaf cats. Furthermore, bilateral deactivation of DZ resulted in the elimination of the enhanced movement detection capabilities of the deaf cats. Deactivation of neither A1, nor AAF, altered performance on either task. Our results show that enhanced visual performance in deaf cats is mediated by cross-modal reorganization within "deaf" auditory cortex and that it is possible to localize and dissociate individual visual functions within reorganized auditory cortex.

Supported by CIHR, NIH and DFG.

Population responses to extended tone stimuli in auditory cortex of awake rats are dominated by global fluctuations

Artur Luczak; Peter Barthó; Kenneth D. Harris
CMBN, Rutgers University, Newark, NJ, USA

The response of auditory cortical neurons to tones is typically strongest at stimulus onset. Analyses of individually recorded neurons show that, for any given tone, a small subset of neurons will fire at elevated rate throughout the tone (the sustained response). From this, one might predict that the population activity that occurs when a tone is played consists of spiking of many neurons at onset, smoothly transitioning to a small number of cells that fire continuously throughout the stimulus.

To examine this prediction, we studied the activity of neural populations in layer V in auditory cortex of awake, head-fixed rats passively listening to one second tones of varying frequencies. Examining the tuning of individual neurons averaged over multiple tone presentations we confirm previous findings, that most cells show only slightly elevated mean rates in the sustained period of any individual tone stimulus. Examination of population activity on a single-trial basis, however, reveals a more complex picture. In both periods of silence and during extended tone presentations, network activity showed large moment-to-moment fluctuations in population firing rate, similar to the up and downstates observed in sleeping and anesthetized animals, but of smaller magnitude. Spiking of (all) neurons was only seen during upstates, both in silence and during tone presentations, and firing rates during upstates were close to those seen at stimulus onsets. The lower firing rates seen during extended tone presentations therefore reflected the low probability of upstate occurrence during extended tones, compared to at stimulus onset. During upstates that occurred in tone presentations, individual neurons showed tuning to stimulus frequency. We suggest that the occurrence of these fluctuations in our inattentive, passively listening subjects may reflect a "gating" process, by which sensory information only reaches auditory cortex during upstate occurrence.

Auditory cortical activity across desynchronized and synchronized states

Marguet, Stephan; Sakata, Shuzo; Curto, Carina; Harris, Kenneth D
Rutgers Univ., Newark, NJ

Low-frequency cortical EEG and alternating periods of neural silence (DOWN states) and activity (UP states) are characteristic of anesthesia and slow-wave sleep. Although tonic firing and high-frequency EEG rhythms ("activated" or "desynchronized" states) are observed during alert wakefulness and REM sleep, these can also be observed under urethane anesthesia spontaneously, or in response to tail pinch or PPT stimulation. We sought to characterize how spontaneous and sound-evoked population activity in the auditory cortex of the urethane-anesthetized rat differed between desynchronized ("activated") and synchronized ("inactivated") states.

In the absence of stimuli, spontaneous firing patterns differed between the two states: most cells exhibited continuous, regular firing during the desynchronized state, characterized by lower Fano Factors. A subset of high-firing cells also showed a high degree of spontaneous rhythmicity, at frequencies between 8 and 18Hz. The broad correlations induced by coactivity during UP states were absent during desynchronization.

Onset response latencies to single click stimuli were similar between states, yielding conserved sequences of activity. In contrast, longer-latency dynamics depended on prior activity during synchronized states, resulting in greater trial-to-trial variability.

We hypothesized that during desynchronized states activity in auditory cortex is under increased external sensory control. To test this hypothesis we predicted spiking activity in response to a frozen amplitude-modulated white-noise (AM noise) stimulus presented during both states. Prediction from the AM noise envelope was best in the desynchronized state. Incorporating simultaneously-recorded population activity or LFPs further improved the prediction, particularly in the synchronized state. These observations suggest that desynchronized states, in which low-frequency oscillatory patterns are suppressed, are more conducive to reliable stimulus coding.

Focusing of acoustic energy on to mechanoreceptor neurons by travelling waves in locusts tympanal ear

T McDonagh, J F C Windmill, S Bockenhauer & D Robert
University of Bristol, UK

In the ear of the desert locust frequency analysis arises from the mechanical properties of the tympanal membrane. Incident sound is spatially decomposed into discrete frequency components through a tympanal travelling wave that funnels mechanical energy to specific tympanal locations, where distinct groups of mechanoreceptor neurones project. Initially, analysis of the travelling waves employed conventional, steady state FFT. This allowed a detailed analysis of the spatial composition of different frequencies onto the membrane. To further understand the exact mechanics of the tympanal travelling wave, its motion was also measured in the time domain to characterise its response to single impulse and single frequency stimuli, with a resolution of 390 ns. This allows the measurement of instantaneous wave velocity and the direct observation of wave compression across the tympanum. A thin region on the tympanal membrane's posterior edge is the collection area for acoustic energy. The apparent function of the subsequent converging travelling waves is to focus kinetic energy from $\sim 2 \text{ nJ/m}^2$ at the start of the travelling wave, to $\sim 12 \text{ nJ/m}^2$ where it terminates at the mechanoreceptor neurone projections. Travelling wave velocities were compared with two competing models of mechanics: the thin-film and stiff-plate models. Wave velocity was found to have limited frequency dependence, thus suggesting that stiffness was not a dominant property of the membrane's mechanics. Therefore, although the locust tympanal membrane exhibits a similar phenomenon to the travelling waves of von Békésy on the mammalian basilar membrane, it appears that the locust travelling wave is not produced by a membrane stiffness gradient, as causes the von Békésy travelling wave.

Sensory-motor integration in primate frontal cortex neurons during a natural vocal behavior: antiphonal calling

Cory T. Miller and Xiaoqin Wang
*Laboratory of Auditory Neurophysiology, Department of Biomedical Engineering,
Johns Hopkins University, School of Medicine*

Through each species' evolutionary history, selection for neural mechanisms that enable each individual to efficiently navigate their social and ecological worlds was critical. Of particular importance are neural processes that integrate incoming sensory information with the resultant behavioral response. While data on sensory-motor interactions in the primate cortex are available, relatively little remains known about this process species' natural behaviors. Here we recorded single-unit activity of frontal cortex neurons in freely-moving common marmoset monkeys (*Callithrix jacchus*) as subjects engaged in a natural (i.e. untrained) behavior known as antiphonal calling. This natural vocal behavior involves the reciprocal exchange of vocalizations. Importantly, the production of an antiphonal call is dependent upon first hearing a particular vocalization, a phee call, and producing the same call type in response. As such, each antiphonal call involves the integration of sensory information with a vocal-motor response. In our first set of analyses, we compared neural activity during each of the three elements of this behavior: sensory period (vocalization presentation), latency delay, and motor response (antiphonal call). The aim here was to determine whether neurons across the population showed firing rate changes during any of these three periods. In our second set of analyses, we examined the effects of behavioral context of the neural response observed during antiphonal calling. Specifically, during test sessions, we presented subjects with vocalizations that did not elicit antiphonal callings and subjects produced vocalizations spontaneously. As such, we tested whether neurons responded similarly during either the sensory stimulus or motor response alone compared to the same sensory or motor period during antiphonal calls. This study builds on our previous work examining the ethology and functional neuroanatomy of antiphonal calling in common marmosets. *This work supported by grants from the NIH to CTM (K99 DC009007) and XW (R01 DC005808).*

Evoked potentials in the macaque auditory cortex after electrical stimulation of the midbrain ventral tegmental area

Judith Mylius¹, Alexander G. Gorkin², Elena Selezneva¹, Henning Scheich¹ and Michael Brosch¹

¹Department of Auditory Learning and Speech, Leibniz Institute for Neurobiology, 39118 Magdeburg, Germany, ²Institute of Psychology, Russian Academy of Sciences, Yaroslavskaya Street 13, 129366 Moscow, Russian Federation

The ventral tegmental area (VTA), which is activated by new stimuli or unpredicted rewards, is part of two major dopamine pathways, namely the mesolimbic and the mesocortical pathway, where dopaminergic neurons in the VTA form widespread projections to the cortex. In general the VTA is associated with stimulus-reward enforced learning; long-term potentiation (LTP) mediated plasticity, affective, motivational, and cognitive functioning and addiction. Bao et al. (2001) were able to show that activity of dopaminergic neurons in the VTA induced a reinforcement of learning-related remodelling of the auditory cortex.

Here we investigated modulatory effects on the activity of the auditory cortex during electrical stimulation of the VTA in the *Macaca fascicularis*. We recorded local slow wave field potentials from auditory cortex and overlying parietal cortex in one unanesthetized animal. Our results revealed similar shapes of the electrically evoked potentials in both cortices, with an early positive component P20 (not always existing), an early negative component N60, a mid-late positive component P80 and a late component at about 120ms. However, evoked potentials had smaller amplitudes in the auditory cortex.

We speculated that the observed early components of the local field potentials were due to direct monosynaptic connections, whereas the mid-late and late components most likely arise from polysynaptic input into the cortex. Our preliminary findings suggest a distinct modulation of adjacent cortical circuits by VTA (dopaminergic) neurons.

Behavioral and autonomic responses to FM sweeps and social calls in awake, restrained mustached bats

R. T. Naumann¹, A. J. Murphy¹, M. S. Mellem¹, B. Wolff¹, *J. S. Kanwal²;

²Dept Physiol/Biophysics; Res. Bldg., Rm WP09A, ¹Georgetown Univ. Med. Ctr., Washington, DC

Bats have been used extensively for studies on auditory processing of social calls. Most of these studies employ awake, restrained animals. We have recently initiated studies of call representation and vocal control within the amygdala of mustached bats, *Pteronotus parnellii*, a highly social and vocal species. Here we examine the response of restrained mustached bats to fear-conditioned frequency modulated (FM) sweeps and to calls, using leg movement, vocalization, and heart rate as response metrics. We recorded the responses of 5 individuals (3 males and 2 females) to a sequence of downward FMs with a 5 kHz bandwidth and a central frequency of 52.5 kHz; (the CS⁺) paired with leg-shock (unconditioned stimulus or US). We also used explicitly unpaired upward FMs with a 5 kHz bandwidth and a central frequency of 32.5 kHz. Both FMs had a slope of 50 Hz/ms. During fear conditioning, either vocalization or movement of the leg receiving the shock was chosen to be the avoidance response. Responses within 5 seconds of CS⁺ onset terminated the CS⁺, resulting in shock avoidance by the trained animal. Three bats responded to CS⁺ presentations with a leg-movement CR, i.e., the shock-paired stimulus evoked enhanced movement compared to an unpaired stimulus (Wilcoxon signed rank, $p < 0.05$). Vocalization was another common conditioned response (CR). One animal avoided shock by vocalizing on 88% of CS⁺ training trials, and vocalized during 76% of non-reinforced CS⁺ presentations (i.e., testing and extinction trials), as compared to 43% of CS⁻ presentations. One exceptional animal exhibited spontaneous echolocating vocalizations when placed in the holder. In this animal, the CS⁺ frequently elicited vocal freezing (suppression of ongoing vocalizations), whereas the CS⁻ elicited an increase in the rate of vocalizations (Wilcoxon signed rank, $p < 0.001$). In addition, the CS⁺ evoked tachycardia in 4 of 5 animals trained with 250 or more pairings. Bats had an average heart rate of 601 (± 48.5 stand. dev.) beats per minute and the CS⁺ evoked an average increase of 2.7%. Changes in heart rate were also used to test the physiological impact of social calls in restrained animals, independent of training. The aggressive rectangular broadband

noiseburst (rBNB) elicited robust changes in heart rate across animals (n = 2), whereas responses to other call types were variable across animals.

Auditory discrimination and brainstem auditory evoked potentials may be affected long term by isoflurane anesthesia in adult rats

J. C. Neill¹, S. J. Gatley²

1Dept Psychol, Long Island Univ., Brookville, NY; 2Pharmaceut. Sci., Northeastern Univ., Boston, MA

In order to assess whether possible impairments in auditory discrimination following irradiation were due to damage to the brain stem auditory pathway, adult male Sprague-Dawley rats were exposed to whole brain radiation with 0, 120, or 240 cGy accelerated iron ions (⁵⁶Fe) of 600 GeV/n at the National Space Radiation Laboratory, Brookhaven National Laboratory. Eight months following irradiation, animals were trained to press a lever for food reinforcement. They were then trained for 12 sessions to discriminate two sounds in a discrete trial successive discrimination using white noise as a cue for reinforcement and a 2 kHz pure tone as a cue for extinction. Then the discrimination was reversed for 12 sessions, followed by a replication of the baseline discrimination. Behavioral results: Significant impairment in auditory discrimination was obtained in irradiated animals, largely in a dose-dependent manner. The number of lever presses made in response to a sound that signaled non-reinforcement were elevated significantly by the reversal condition in a dose-dependent manner. The irradiated animals also showed a significant HZE dose-dependent impairment in discrimination of a silent discriminative stimulus for extinction. A BAEP (Brainstem Auditory Evoked Potential) was obtained for both left and right ears of each animal. Latencies were defined as the amount of time from stimulus onset until the crest of waves I, II, III, and IV, which were peaks in voltages identified manually. BAEP results. Threshold was defined as the lowest level at which responses were clearly observed at waves I, II, III and IV. BAER threshold was estimated with a 5-dB resolution from 0 to 80 dB SPL. The HZE-irradiated were markedly impaired in adjusting their levels of discrimination responding based on auditory stimuli. Of interest, some variability in thresholds was correlated with anesthesia. There was a highly positive correlation (up to .88) between the duration of isoflurane anesthesia (administered at concentration of 4%) and the latency of wave IV in control animals, suggesting that this factor of isoflurane anesthesia may have inadvertently contributed to auditory discrimination impairments in the overall experiment. Investigators should be alert to the possible long term contribution of isoflurane anesthesia to behavioral and BAEP results.

Effect of reversible inactivation of different auditory cortical areas on plasticity of sound localization in adult ferrets

Nodal F. R., Bajo V. M. & King A. J.

Department of Physiology, Anatomy and Genetics, University of Oxford, UK

The auditory cortex plays a key role in sound localization, shown by the contralateral deficits produced when it is lesioned or inactivated. We trained adult ferrets by positive conditioning to localize broadband noise across the full 360 degrees of azimuth (angular resolution 30 degrees), recording both the approach to target and initial head orientation responses. To explore the contribution of different auditory areas to normal sound localization and to the ability of the animals to relearn to localize sound accurately following insertion of an earplug in one ear, we reversibly inactivated different auditory areas by subdural placement of a polymer that released muscimol over a period of weeks. The release polymer was placed bilaterally over the anterior, middle or posterior ectosylvian gyrus (EG) in different animals. Contrary to other studies, inactivation of any region of the EG did not have a particularly marked effect on localization ability, as assessed by either the approach to target or head orienting responses, which were comparable in accuracy to those observed before and after implantation, especially at long sound durations. After insertion of a unilateral ear plug, control animals exhibit a large deficit in localization accuracy in the approached to target task, particularly on the ipsilateral side, but, with appropriate behavioural training, performance recovers over the next few days. Similarly the correlation between the head orientation responses and the location of the target

was disrupted mainly in the ipsilateral side, with responses showing a correct directionality but lesser amplitude, effect that recovered partially with training. However, we found that inactivation of any of the three main regions of the EG, resulted in less complete and slower adaptation to the ear plug than in controls. The effects on adaptation were similar regardless of the areas inactivated suggesting that the integrity of each of these regions of the auditory cortex is needed to achieve a complete adaptation to altered localization cues in adult animals.

Voice region connectivity in the monkey assessed with microstimulation and functional imaging

C. I. Petkov¹, Y. Kikuchi^{2,3}, M. Augath¹, M. Mishkin³, J. P. Rauschecker² & N. K. Logothetis¹

¹*Dept. Physiol. of Cognitive Processes, Max Planck Inst. for Biol. Cybernetics, Tübingen, Germany;*

²*Dept. Physiol. & Biophysics, Georgetown Univ. Med. Ctr., Washington, DC, USA;* ³*Lab.*

Neuropsychology, NIMH, NIH, Bethesda, MD, USA.

A “voice” region has recently been identified in the monkey auditory cortex with functional magnetic resonance imaging (fMRI) and electrophysiology, which shows a close functional correspondence to the known human-voice region. Both human and monkey voice regions lie anterior and superior on the temporal lobe and strongly prefer species-specific vocalizations over other categories of sounds and acoustical controls. The human and monkey voice regions are also sensitive to the vocal differences among individuals and appear to be important centers for vocal sound processing within a network that is poorly understood. To clarify the in-vivo functional connectivity of the voice region in the rhesus monkey we used microstimulation in combination with high-resolution fMRI. First we functionally localized the voice region with blood-oxygen-level-dependent (BOLD) fMRI, as previously described. Then we microstimulated the voice region with glass-coated iridium microelectrodes, using biphasic, cathode leading, 250 to 500 μ A pulses of 200 μ s duration. We used the BOLD response to evaluate the anterograde targets of the microstimulation site. Microstimulation of the monkey voice region, which lies on the rostral superior-temporal plane (rSTP), elicited a BOLD response from hierarchically earlier auditory areas (feed-back), and the surrounding superior temporal plane (STP), gyrus (STG) and sulcus (STS) of the ipsilateral hemisphere. We observed no direct targets in the prefrontal cortex from voice region microstimulation, so we hypothesized that voice information might reach the frontal cortex indirectly. To test this idea we microstimulated a region in the upper bank of the STS that was one of the direct targets of the voice region, which resulted in medial and orbital prefrontal cortex activity, and neighboring regions on the STP, STG, STS and temporal pole. Our initial observations suggest that acoustical information from the voice region reaches the frontal cortex indirectly via other rostro-temporal regions such as the STS. Since the primate STS receives multisensory input and is known to contain face-recognition regions, we propose that voice information is paired with face information in the anterior temporal lobe before being transmitted to the prefrontal cortex.

Support: Max Planck Society (NKL, CIP), Alexander von Humboldt Foundation (CIP), NIH-R01 NS052494 (JPR, YK), NSF PIRE OISE-0730255 (JPR, YK), NIMH, NIH (MM).

Functional Imaging of Sensitivity to Components of the Voice in Monkey Auditory Cortex

Christopher I. Petkov^{1*}, Christoph Kayser¹, Asif A. Ghazanfar², Roy D. Patterson³ & Nikos K. Logothetis^{1,4}

¹*Max-Planck Institute for Biological Cybernetics, Tübingen, Germany;* ²*Princeton University, New Jersey, USA;* ³*University of Cambridge, Cambridge, UK;* ⁴*University of Manchester, Manchester, UK*

A voice region has recently been identified in the monkey auditory cortex which prefers species-specific vocalizations and is sensitive to the vocal differences among monkey callers. To better understand the sensitivity of this and other brain regions for species-specific vocalizations, we independently manipulated two components in monkey vocal sounds. After recording the ‘coo’ vocalizations from 4 rhesus monkeys, we either shifted the position of the fundamental frequency (which is established by the vocal source in the larynx) or shaped the dispersion of the higher, formant frequencies (established by the acoustical filtering that occurs in the vocal tract above the larynx). The

manipulations left the sounds within the species-typical range. We then used high-resolution functional imaging (fMRI) to evaluate the sensitivity of the rhesus monkey brain to independent changes of the two vocal components. Initial results revealed that many regions along the auditory-cortical processing hierarchy were sensitive to changes in both the fundamental and formant frequencies. In the earlier stages of cortical processing, especially in the caudal auditory regions, the sensitivity of the auditory fields to changes in the fundamental and formant frequencies depended upon each field's topography of preferred sound frequency (tonotopy), which we mapped separately. For example, the sensitivity of the auditory field A1 to manipulation of the fundamental frequency occurred over this field's low-frequency region, while the sensitivity to manipulation of the higher formant frequencies occurred over its high-frequency preferring region. The sensitivity of the anterior cortical regions to the components in the voice showed no such dependency upon their tonotopy. Notably, the monkey voice region, near to the temporal pole, showed better sensitivity to changes in the formant frequencies than to the fundamental. The results reveal a putative cortical network for vocal-sound processing and suggest that the voice region extracts information about speaker identity from cues present in the formant frequencies.

Funding Sources: Max Planck Society (CIP, CK, NKL); Alexander von Humboldt Society (CIP); UK Medical Research Council (G9900369, G0500221) (RDP); NIH R01NS054898 (AAG); NSF BCS-0547760 CAREER Award (AAG)

Responses of the neuronal population to natural and synthetic sounds in rhesus monkey auditory cortex

*M. Ortiz, P. Kusmierek, J. P. Rauschecker

Interdisciplinary Program in Neuroscience, Georgetown Univ., Washington, DC; □Department of Physiology & Biophysics, Georgetown Univ., Washington, DC

The auditory cortex plays an important role in processing of sounds, which ultimately leads to auditory stimulus categorization. Neural mechanisms in the auditory domain for such categorization still need to be revealed. We collected responses from a large number (>400) of neurons in the left auditory core and medial belt fields of two awake rhesus monkeys working in a simple auditory discrimination task. The animals were presented with natural sounds that belonged to intuitive, possibly behaviorally relevant categories: ten monkey calls and ten environmental sounds, which were recorded in the monkeys' housing area. In addition, we presented synthetic stimuli: pure tones (PT) and band-pass noises (BPN) of 1/3-octave and 1-octave bandwidth. The BPN center frequencies were matched to the PT frequencies, spanning 0.125-32 kHz. All stimuli were played at ~50 dB above hearing threshold. We analyzed mean firing rate from the following temporal windows: on (stimulus onset + 100ms), sustained (from 100 ms after onset to offset) and off (offset + 100ms), and their combinations. For each pair of sounds we calculated the correlation coefficient (r) between firing rates elicited in the neuronal population. A dissimilarity matrix based on neural distance ($1-r$) was a substrate for multidimensional scaling (MDS) and hierarchical clustering methods employed to reveal clustering of the response patterns to sound stimuli. Using MDS we observed that most of the classification structure could be derived from the "sustained+off" response window, whereas information in the "on" window failed to yield a clear and explainable cluster structure. Using hierarchical clustering on the "sustained+off" window we found that natural and synthetic sounds created distinguishable clusters. The natural sounds were further divided along the monkey- calls/environmental-sounds division. Synthetic sounds grouped into clusters depending on the center frequency, but no separation was observed between BPN and PT. Although the clustering appeared to be explainable mostly by the acoustic structure of the stimuli, our results indicate that activity of the neuronal population at a relatively low level of auditory cortical processing carries sufficient information to support classification of sounds into major classes.

Cortical mechanisms for segregating and integrating auditory objects

Tobias Overath, Sukhbinder Kumar, Lauren Stewart, Katharina von Kriegstein, Rhodri Cusack, Adrian Rees, Tim Griffiths

Functional Imaging Lab., Univ. Coll London, London, United Kingdom; Med. Sch., Newcastle Univ., Newcastle upon Tyne, United Kingdom

The ability to hear out a single voice in a noisy gathering is a sophisticated process in which the brain far surpasses the performance of machines. To achieve this, we must identify the many frequency-varying elements in sounds that constitute a single voice or auditory object, whilst also detecting the boundaries that distinguish the voice from other objects. Here we considered the cortical bases for these two fundamental processes using a novel stimulus (an 'auditory texture') in which auditory object salience and boundaries between objects were manipulated independently. Each auditory object was identified by the percentage of randomly distributed frequency-modulated (FM) ramps that had identical direction and trajectory (spectrotemporal coherence), while boundaries were introduced by juxtaposing auditory objects of different coherence levels. Using functional MRI (fMRI), we show that mechanisms defining object boundaries (changes in coherence) are represented in primary and association auditory cortex. In contrast, the representation of the salience of the object (percentage of coherence) occurs only in auditory association cortex. Furthermore, participants' superior detection of boundaries across which coherence increased was reflected in a greater neural response at these boundaries. The anatomical organisation revealed by these results suggests a hierarchical mechanism for the analysis of auditory objects: boundaries between objects are first detected as a change in statistical coherence over frequency-time space, before a representation that corresponds to the salience of the perceived object is formed.

Neuronal activity in primate prefrontal cortex during performance of an auditory delayed matching-to-sample task

Bethany Plakke¹, Amy Poremba^{1,2}, Chi-Wing Ng¹, and Ryan Opheim¹.

1Department of Psychology, Division of Behavioral and Cognitive Neuroscience, University of Iowa, Iowa City, IA 52242, 2Neuroscience Program, University of Iowa, Iowa City, IA 52242.

Both imaging and neurophysiological recording studies have demonstrated that the prefrontal cortex (PFC) is responsive to auditory stimuli (e.g., Poremba et al., 2003; Romanski & Goldman-Rakic, 2002). Additional work has shown the PFC is involved in tasks requiring working or short-term memory (e.g., Bodner et al., 1996; Fuster, 2000; Warden & Miller 2007). Here, we examine rhesus macaques on an auditory go/no go delayed matching-to-sample (DMTS) task wherein two acoustic stimuli (500 ms), separated by a fixed memory delay (5000 ms), were either identical sound presentations, or two different sound presentations. A small candy reward was delivered after a correct button press on match trials. Each training session consisted of 200 trials, where half the trials were match trials and half were nonmatch trials. The sound stimuli for each recording day were 8-10 sounds chosen from a larger sound set. Each sound was repeated at least 8 times on both match and nonmatch trials within a recording session. The sound stimuli included pure tones, frequency sweeps, man-made environmental sounds, monkey vocalizations, natural sounds, synthesized sounds, and other animal sounds. After reaching a criterion of 80% correct or better on the behavioral task recording wells were implanted over the left lateral bank of the principal sulcus in prefrontal cortex and recording sessions began. Assessment of neuronal firing rates and waveforms was completed for task related activity, as well as for the same sound stimuli during passive listening. Preliminary results from one female monkey indicate that cells in this area are responsive to complex auditory stimuli in a selective manner. Additionally, there are some single-units that fire more during the delay period correlated with behavioral performance. Examination of individual sounds presented during match trials associated with correct versus incorrect behavioral performance revealed single units with higher firing rates during correct match performance to the sound stimuli than on incorrect match trials. Some of these same single-units displayed a higher frequency of spike firing during the delay period for incorrect match trials compared to correct match trials for the same sound stimulus. Preliminary data indicate that this region, which receives auditory input from the superior temporal gyrus, is encoding complex auditory stimuli and may also be active during the delay memory period under specific conditions. *Support: Startup funds from the Univ. of Iowa and NIDCD grant DC0007156 to A.P.*

Effects of sound duration on the neural responses of the primary auditory cortex in awake cats

L. Qin, J. Wang, Y. Sato

Dept Physiol, Univ. Yamanashi, Chuo, Japan

Acoustic perception highly depends on the sound duration. A tone shorter than 4ms is usually perceived as a click without a clear pitch. A sound quality of a sinusoid with salient pitch only appears when the tone duration is longer than 10ms. The related neural mechanism remains unknown. Here, we explore this issue by examining the neuronal responses to the tone bursts with different durations (0.5-320ms) in the primary auditory cortex (A1) of awake cats. Neurons exhibited two distinct temporal response patterns to 320ms duration tones. One is the phasic response synchronizing to the stimulus onset and offset. The other is the sustained response continuing throughout the stimulus duration. The two response patterns may characterize two distinct cell groups in A1, because the change of sound duration had different effects on the phasic and sustained response cells. The onset response of phasic cells showed up a similar shape and peak amplitude to all the tones of 0.5-320ms, while, the offset response is only observable when the stimulus duration was longer than 40ms. On the other hand, the change of duration from 40 to 320ms had less effect on the cells with the sustained response, except for the extension of response duration. However, the decrease of stimulus duration from 40 to 0.5ms caused a continuous and substantial decrease in the response amplitude. Since a click-like tone can only evoke a vigorous response in the phasic cells but not in the sustained cells, the former may serve more to constitute the click perception. The sustained cells, which are fully activated only by the longer tones and can continuously track the stimuli, may play a major role in tonal perception. Thus, the duration-dependent acoustic perception may be attributable to the duration-dependent shift of working neurons in A1. Our electric physiological findings also explain why the durations <40ms are more difficult to be discriminated for the human subjects than those >40ms. That is, the durations > 40ms can be discriminated by both the response duration of sustained cells and the offset response of phasic cells, whereas, the duration <40ms, only by the response amplitude of sustained cells.

This work was supported by National Nature Science Foundation of China under Grant (No.30700938) and Grant-in-Aid for Scientific Research B (No.20300076) from Japan Society for the Promotion of Science (JSPS).

The role of electrical synapses in the processing of sensory information

Paulo Vianney Rodrigues^{1,2*}, Dan Iancu¹, Eric Washburn¹, John Welsh²

1.Oregon Health Science University, Physiology/Pharmacology Dept.

2.Drexel College of Medicine, Pharmacology/Physiology Dept.

Electrical synapses are mediated by channels known as gap junctions, which are formed by oligomerization of connexin 36 (CX36) proteins in neurons. Recently, we developed a lentivector that carries a dominant negative form of the CX36 which blocks the generation of electrical synapses. Experimental evidence collected in intracellular recordings in vitro support the hypothesis that the role of electrical synapses is to synchronize neuronal networks at specific frequency bands to process sensory information. We directly tested this hypothesis by infecting a large neuronal population with the lentivirus carrying the mutated CX36 and recording auditory evoked potentials induced by 10 KHz pure tones played at 70 db in the auditory cortex of awake rats. We also recorded the LFP activity of uninfected rats and rats infected with an innocuous lentivector carrying the gene of the Green Fluorescent Protein. We then performed spectral analysis of these three LFP data sets. Our preliminary results indicate that the LFP spectrograms of these three experimental groups are overall similar. However, the power spectral density of the LFP shows that there is a 10 fold decrease in the power across a wide frequency range in the LFP of rats injected with the mutated CX36. Our preliminary results also indicate that there is a decrease in coherence at alpha, beta, and gamma frequency bands in these rats. To our knowledge, this is the first experimental evidence suggesting that electrical synapses underlie a temporal code for the processing of sensorial information in awake rats.

Spike distance analysis of AM processing in auditory cortex: correlates to behavior

Rosen MJ, Semple MN, and Sanes DH

Center for Neural Science, New York University

The emergence of mature temporal processing is essential for a broad range of auditory tasks, from sound localization to communication. Surprisingly several auditory percepts develop quite slowly. For example, human sinusoidal amplitude modulation (sAM) detection thresholds take more than a decade to mature. However, there is little understanding of the developmental trajectory of central neuronal coding properties that might limit behavioral performance. Using an awake, developing gerbil model, we have studied the development of auditory cortex neuronal coding properties for sAM tones, and have compared this neural coding with behavioral performance in adults. Single unit extracellular recordings were obtained in young (~P30) versus adult (>P60) gerbils in response to sAM stimuli of varying modulation depths (with a carrier at each cell's CF, and 2 - 5 Hz modulation frequency). A spike distance analysis was used to determine the neural time scale that provides the most information contributing to sAM detection thresholds (Victor & Purpura '97). For example, if firing rate is important for detecting sAM, this predicts that within either age group, spiking patterns distinguishing sAM from non-sAM background should differ at longer, rate-based timescales rather than shorter timescales. The spike-distance analysis revealed that this was indeed the case for both adults and young (where maximum attainable information is 1): for adults, the maximum information available at the longest (1 sec) time scale was 0.666 ± 0.006 , whereas it dropped to 0.362 ± 0.006 by 12 ms. For young, the 1 sec time scale information was 0.496 ± 0.004 and dropped to 0.185 ± 0.003 by 12 ms. These data also demonstrate that, for a given time window, maximum information is lower for young animals. If a neural rate code is being utilized, we would predict that adult behavioral thresholds would best match neural thresholds based on long time windows. We will present an analysis that compares cortical discrimination ability at various time scales with adult behavioral psychometric functions for sAM depth detection. Preliminary analyses show that fine time scales (<10msec) do not provide enough information to support adult performance. Additionally, spike trains from young animals are less able to distinguish sAM from background at all timescales than are adult neurons. Therefore, we would predict that young animals would show poorer performance on this sAM detection task than adults (see Sarro et al, this meeting). Our results indicate that central coding of stimulus envelope displays a prolonged period of maturation, and may limit the perceptual abilities of developing animals. *Supported by NIH 1F32DC009165 and an NOHR Research Award to MJR.*

Vocal Control during Acoustic Interference in Common Marmosets

Sabyasachi Roy, Cory T. Miller, Dane Gottsch and Xiaoqin Wang

Dept of Biomedical Engineering, Johns Hopkins University, Baltimore, MD

Vocal communication is an essential part of social behavior in organisms such as primates, amphibians, birds and insects. The natural acoustic environment of vocal species inherently contains noise that can be periodic or unpredictable in nature. The ability of both human and nonhuman species to avoid intermittent acoustic noise during vocal communications is critical for maintaining the communicative efficacy of the signals. Although it has been shown that some species possess mechanisms that enable them to avoid acoustic interferers when producing vocalizations, little is known about this issue in nonhuman primates. Here we tested the ability of a New World primate, the common marmoset (*Callithrix jacchus*), to control the timing of vocalizations during antiphonal calling interactions in a controlled acoustic environment. We examined the vocal behavior of marmosets in three different controlled noise conditions: white noise pulses with periodic silent gaps, white noise pulses with predictable silent gaps and white noise pulses with unpredictable silent gaps. We observed that the majority of the calls were initiated during silence and that marmosets were able to modify the timing of the calls according to the given noise environment. Moreover, the duration between the call-onset time and the end of the preceding noise pulse decreased with shorter silence gaps. In the predictable noise condition, the marmosets precisely controlled their call onset time in

order to complete the call within the silence gap. Overall, these findings suggest that marmoset vocal behavior is an attractive model to study the neural basis of vocal control and feedback.

Acoustic feature analysis in the primary auditory cortex

Srivatsun Sadagopan & Xiaoqin Wang

Dept. of Neuroscience and Dept. of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore MD 21205

Many neurons in the primary auditory cortex (A1) of awake marmosets were found unresponsive to pure tone stimulation (112/460, ~25%). However, many of these neurons were driven by auditory stimuli: they selectively responded to specific features present in marmoset vocalizations and environmental sounds. In order to identify the computations underlying this feature selectivity, we developed an input-based description of these neurons using a modified two-pip stimulus paradigm. We observed that nonlinear, local and precise combinations of two tone-tuned inputs with specific frequency and time differences between them could explain the observed responses to complex stimuli. These neurons, located mostly in the superficial layers of A1, could form a putative low-level feature-detection stage of auditory processing. Next, we asked how well such nonlinear receptive fields performed in simulations of a vocalization discrimination task. Using acoustic analyses of marmoset vocalizations, we quantified information contents of various receptive field (RF) models, including pure-tone, two-pip, call-fragments, whole-call templates, average-call templates and noise RFs in the context of vocalization classification using an information-maximization approach. We found that RF models based on the physiologically observed two-pip RFs exhibited intermediate information contents, between pure-tone (low) and call-fragment (high) RFs. Interestingly, because of the high variability in marmoset vocalizations, whole-call and average-call templates performed worse than pure-tones. Call fragments, consisting of local spectro-temporal features, exhibited the best information contents, a novel prediction that may be physiologically tested. These results indicated that two-pip RFs exhibited high selectivity for useful local features, but not at the expense of generality, such that two-pip like RFs could potentially form a useful next step in the auditory processing hierarchy in the context of an ecologically relevant task. Our results suggest a processing hierarchy in auditory cortex, with features of increasing complexity being extracted progressively from sounds at higher processing stages.

State dependence of laminar processing in the auditory cortex

Shuzo Sakata and Kenneth D. Harris

Center for Molecular and Behavioral Neuroscience, Rutgers University

197 University Avenue, Newark, New Jersey 07102, USA.

Smilow Neuroscience Program and Department of Otolaryngology, New York University School of Medicine, 550 1st Avenue, New York, New York 10016, USA.

Neocortical circuits show distinct states, such as the desynchronized state during waking and REM sleep, and the synchronized state during slow-wave sleep and anesthesia. How the states differently modulate activities of diverse cell-classes is poorly understood. Here we show state-dependent and cell-type specific modulation of neuronal activity in the primary auditory cortex. We used the juxtacellular method to identify morphological classes, simultaneously with large-scale extracellular recording to monitor population activity of single cells across cortical layers. The desynchronized state was induced under urethane anesthesia by electrical stimulation of the pedunculo-pontine tegmental nucleus or basal forebrain. The effect of desynchronization on baseline firing rates varied both between and within morphological classes. In layer 2/3, most pyramidal cells were suppressed by desynchronization, whereas layer 5 thick pyramidal cells typically increased their rates. Layer 4 pyramidal cells and layer 5 slender pyramids showed within-class variability, but with a slight tendency towards suppression; layer 6 pyramids were diverse. Overall, the change in baseline rate was predictable from the neuron's baseline rate during the synchronized state, with neurons of high spontaneous rate exhibiting further increases on desynchronization. For all cells, spontaneous spiking

during synchronized states was exclusively restricted to "up-states" of global activity seen at the population level; up-states do not always drive the superficial layers. During the desynchronized state, this pattern was replaced by tonic and largely uncorrelated spiking in the deep layers, with generalized neuronal silence in the superficial layers. In the synchronized state in at least pyramidal cells of all layers, therefore, spiking reflects an interaction of spontaneous and sensory-evoked activity; desynchronization may improve the detectability of sensory information by suppressing the globally correlated dynamics. *Supported by NIH grant (1R01MH07324501), Alfred P Solon Foundation (KDH), and the Sound Technology Promotion Foundation (SS).*

Juvenile training enhances adult performance on an auditory perceptual task

Emma C. Sarro, Jack B. Kelly, Dan H. Sanes

Ctr. Neural Sci., New York Univ., New York, NY; Carleton Univ., Ottawa, ON, Canada

A general theory of sensory development holds that early experience can influence central nervous system function, thereby shaping adult perceptual skills. If so, then we would expect juvenile training on an immature auditory perceptual task to improve adult performance. We tested this idea in gerbils by examining the maturation of sinusoidal amplitude modulation (sAM) detection, a percept that displays a prolonged maturation in humans (Hall and Grose, 1994; Banai et al., 2007). We first assessed the normal rate of maturation. Animals were trained and tested on an sAM detection task as early juveniles (P25-37), late juveniles (P40-55) and as adults (P70-85). Initial detection thresholds were obtained by presenting each animal with the full range of sAM depths (0-100%) in random sequence. Following this, best detection thresholds were acquired over several days by testing with a range of sAM depths that bracketed an animal's detection threshold from the previous day. The best sAM detection thresholds continued to improve throughout late juvenile development ($40\pm 4\%$ at P30, $27\pm 2\%$ at P40, $22\pm 2\%$ as adults), similar to that observed for humans. For a given initial detection threshold, adults displayed larger improvements during the period of testing, as compared to juveniles. We then asked whether active training during development can influence adult performance. sAM detection was assessed in adult animals following either of two juvenile treatments: (1) auditory training on sAM detection or (2) procedural training only (i.e., learning to drink from the water-spout without auditory training). The results indicate that auditory training in juveniles improves the best threshold displayed by adults (procedural training: $22\pm 2\%$; P30 sAM training: $17\pm 1\%$; P40 sAM training: $13\pm 1\%$). Thus, adult behavioral performance can be modified by actively training animals at an age when their perceptual skills are quite immature.

Response complexity and encoding of stimulus contrast in primary auditory cortex of the awake ferret

B. Shechter, Y. Ji, D.A. Depireux

Anat. and Neurobio., Univ. of Maryland Sch. of Med., Baltimore, MD

The responses of auditory neurons are often characterized by their spectro-temporal receptive field (STRF). This linear measure has been shown to capture the overall trend of the response, but by nature of its construction, it does not reflect any nonlinear processing. We have recently shown that neurons in primary auditory cortex (AI) of the awake ferret respond with non-trivial nonlinearities (not solely the result of rectifying or saturating nonlinearities). Using reverse correlation techniques with respect to the spectro-temporal envelope of auditory gratings (or ripples), we reveal phase-dependent contrast tuning in single units. One of the assumptions in the STRF model is that the mean firing rate (averaged over any single period of the stimulus) does not depend on the spectro-temporal modulations, but rather on the overall level of the stimulus. This phase-independent contrast tuning is analogous to complex visual neural responses, in which responses to a grating stimulus do not depend on its spatial phase. We investigate the existence of phase-dependent vs. phase-independent complex responses to the contrast of auditory stimuli.

Natural-sound-evoked and tone-evoked receptive fields in songbird auditory midbrain neurons

David M. Schneider¹ & Sarah M.N. Woolley²

¹*Doctoral Program in Neurobiology and Behavior, Columbia University*

²*Department of Psychology & Center for Neurobiology and Behavior, Columbia University*

Receptive fields estimate the neural filters of sensory neurons and can be used to predict neural responses to novel stimuli. The spectral tuning properties of auditory neurons are traditionally characterized using pure tones of varying frequencies and intensities to calculate tone-evoked receptive fields (RFs). Alternatively, spectrotemporal receptive fields (STRFs) calculated from neural responses to complex sounds can be used to characterize both the spectral and temporal tuning properties of auditory neurons. Here, we compare tone-evoked RFs to STRFs obtained using complex natural and artificial sounds, zebra finch song and modulation-limited noise. We recorded spiking activity from single neurons in the zebra finch midbrain and computed tone-evoked RFs and separate STRFs from responses to songs and noise samples. Song and noise STRFs reliably capture the characteristic frequency of auditory neurons predicted by tone-evoked RFs. Noise STRFs either match or under-estimate the tone-evoked bandwidth, while song STRFs either match or over-estimate the tone-evoked bandwidth. Importantly, song STRFs predict the neural response to novel songs better than do noise STRFs or tone-evoked RFs. Furthermore, we observed stimulus-specific responses that would not be predicted by tone-evoked RFs. These data indicate that STRFs derived from responses to natural sounds accurately estimate the neural filters of auditory neurons.

Neural correlates of rhythmic masking release (RMR) in auditory cortex of the awake monkey.

M. Steinschneider and Y. Fishman.

A. Einstein Coll. of Med., Bronx, NY 10461.

RMR is one of the most powerful demonstrations of auditory scene analysis. In RMR, perception of a simple rhythm heard when a regular sequence of sounds is played in isolation is interrupted when an added sequence of identical sounds (“maskers”) is intermingled with the rhythm. Perception of the original rhythm is restored by adding “flanker” sounds in frequency regions adjacent to the “maskers”. RMR is maximal when “maskers” and “flankers” are synchronous and spectrally similar.

We examined response patterns in auditory cortex potentially relevant for RMR. Tone sequences (“rhythm”) were presented and later disrupted by the introduction of additional tones (“maskers”) of identical frequency. “Rhythm” and “masker” tones were spectrally near the best frequency (BF) of recording sites. “Flanker” tones simultaneous with the “maskers” were subsequently added to the sound sequences and the neural responses compared across conditions. “Flankers” were varied in their frequency separation from the “maskers”. Additional tone sequences that modeled response patterns as “viewed” by sites with BFs near the “flanker” frequencies were also presented.

Neural patterns were identified that might serve as neural correlates of RMR. These included patterns wherein responses evoked by the “maskers” were suppressed when simultaneous “flankers” were presented, thus accentuating responses evoked by the “rhythm”. Suppression was often more pronounced when “flankers” were spectrally adjacent to the “maskers”, in accordance with perceptual findings. An additional pattern was observed when examining responses evoked by tone sequences that modeled activity as “viewed” by sites where “flankers” were near the BF of recording sites. Here, responses with different spatial activations across auditory cortex were observed for the “rhythm” and “masker-flanker” combination, respectively.

We conclude that temporal and spatial patterns of auditory cortical activity may underlie the perceptual phenomenon of RMR. *Supported by DC00657.*

Pitch discrimination thresholds as a function of task design

Kerry M. M. Walker, Jennifer K. Bizley, Andrew J. King & Jan W. H. Schnupp

Department of Physiology, Anatomy and Genetics, University of Oxford, UK

Previous studies of frequency discrimination have measured animals' performance on "go/no-go" tasks in which the subject is required to respond to a change in tonal frequency. Weber fractions on these tasks, calculated as the just noticeable difference in frequency as a fraction of the reference frequency, have generally been found to vary from 1-10% in mammals such as cats, chinchillas, gerbils, and rats. We have measured the ability of ferrets to discriminate the frequency of tones and the pitch of artificial vowel sounds using a 2-alternative forced choice (2AFC) design that more closely resembles studies of human frequency discrimination. We found that performance on this task (Weber fractions = 20-60%) was considerably poorer than that reported for other species in earlier studies. There are at least two explanations for the poorer performance measured on our task. First, while previous studies simply required animals to detect a change in tone frequency, our tasks required ferrets to report the direction of pitch change between sounds. Second, animals have been shown to discriminate the quality of sounds better on tasks with go/no-go than 2AFC designs, although explanations of this well-documented phenomenon remain speculative (Burdick, 1979, *J. Aud. Res.* 19:59-82). To examine possible effects of perceptual and cognitive demands on pitch discrimination performance at the cortical level, we designed "neurometric" algorithms to discriminate the pitch of artificial vowels (i.e. bandpass-filtered click trains) based on the responses of ferret auditory cortical neurons. We show that up to 89% of simultaneously recorded neural populations support better pitch discrimination performance on change detection tasks designs than on analogous pitch direction judgment tasks. Neurometric results are compared to behavioural measurements of ferret pitch discrimination using 2AFC and go/no-go tasks. The results emphasize the importance of task design in auditory discrimination studies, in both psychophysical experiments and neurophysiological investigations.

Rate Regulation of Sound Level Encoding in Auditory Cortex

Paul V. Watkins, Dennis L. Barbour

Department of Biomedical Engineering, Washington University, St. Louis, MO, USA

The recent history of stimulus statistics alters response properties of many sensory neurons on short time scales—a neuronal characteristic typically referred to as adaptation. We previously used an adaptation-inducing stimulus paradigm to demonstrate that neurons responding nonmonotonically to sound level (i.e., "level tuned") preferentially adapt the positive slope of their input/output functions to improve coding accuracy. Additionally, nonmonotonic neurons adapt the most in response to stimuli that contain predominantly low sound levels. In contrast, neurons responding monotonically to sound intensity adapt equally well at low and high sound intensities. Adaptation of nonmonotonic neurons may reflect a joint coding strategy whereby the positive slope of nonmonotonic rate-level functions encodes the lowest stimulus levels to which the organism is sensitive and the negative slope preserves this high sensitivity when relatively rare but intense events occur that would otherwise desensitize these neurons temporarily. Neural responses as a function of the current and the preceding level demonstrate separability for nonmonotonic but not for monotonic neurons, implying that rate regulation in nonmonotonic neurons is mostly due to a gain effect, whereas monotonic neurons shift their input/output functions in order to regulate rate. Using a modified version of the adaptation paradigm in auditory cortex of awake monkeys, we demonstrate a distinction between mechanisms of rate regulation to varying sound level statistics in nonmonotonic versus monotonic neurons that has potential significance for preserving sensitivity while encoding a wide dynamic range.

Effects of microstimulation of prefrontal cortex on neural activity in auditory cortex

Daniel E. Winkowski, Pingbo Yin, Jonathan B. Fritz, Shihab A. Shamma

Neural Systems Laboratory, Institute for Systems Research, University of Maryland, College Park 20742

A majority of neurons in the primary auditory cortex selectively adapt to the presence of salient cues in auditory tasks by rapidly changing their neural response properties (i.e., spectrotemporal receptive field (STRF) properties; see Fritz et al., 2003). Presumably these changes are the result of signals

originating in higher cortical areas. Currently, our knowledge regarding the source of those signals is limited. The prefrontal cortex (PFC) is one such area that is known to play an important role in attentional task performance and therefore, may have a role in modulating auditory cortical responses. We explored whether electrical microstimulation of the PFC can modulate neural responses in the auditory cortex of awake, passively listening ferrets. We measured auditory cortical neural activity in response to a range of auditory stimuli (i.e. either pure tones or temporally orthogonal ripple combinations) in the awake, non-behaving ferret and compared those responses with neural responses measured while electrical microstimulation was applied to a site in the PFC. Electrical microstimulation of the PFC was paired with a pure tone of a single frequency that was within (or outside) the receptive field of the neuron. We recorded single units in primary auditory cortex of 2 ferrets and preliminary results suggest that neural activity in the auditory cortex can be modulated by low-amplitude microstimulation of the PFC. We shall describe the effects of the PFC electrical microstimulation/pairing manipulation on activity of auditory cortical neurons as well as the effects on the frequency tuning and spectrotemporal receptive field properties of the neurons in the auditory cortex.

Functional microcircuits in neonatal auditory cortex before and during the onset of hearing

Cuiping Zhao, Sharba Bandyopadhyay, Patrick O Kanold

Department of Biology, Institute for Systems Research, Program in Neuroscience and Cognitive Science; University of Maryland, College Park, MD 20742

The functional connectivity of the primary auditory cortex (A1) is shaped by experience during development, especially during a critical period early in life. During early times in development, additional neuronal circuits, formed by subplate neurons (SPNs), are present in the prenatal and neonatal cortex that are absent in the adult cortex. Despite the demonstrated importance of SPNs in functional maturation of cortical circuits, little is known about how these neurons are integrated in the developing thalamocortical circuit. We addressed this question physiologically by studying SPN in vitro in thalamocortical slices of A1 and medial geniculate nucleus (MGN) in mouse from postnatal day (P) 3 to P15. Using electrical stimulation of the thalamocortical projections we find that SPNs receive functional excitatory inputs from MGN as early as P3. MGN projections to SPNs are glutamatergic, are transmitted by both NMDA and AMPA receptors, and strengthen between P3 and P15. MGN inputs to SPN were capable of inducing action potentials in SPNs suggesting that SPNs are tightly integrated into the developing thalamocortical circuit and that they can receive early spontaneous and later sound driven activity. We tested this hypothesis directly by recording single unit activity in awake neonatal mice and found that putative SPNs show sound driven neuronal activity. Photostimulation of SPNs revealed excitatory projections from SPNs to developing layer 4, the target of MGN projections. Thus SPNs are tightly integrated into the developing thalamocortical circuit. These results suggest that SPNs are a reliable relay of early spontaneous and sound evoked activity to the developing auditory cortex. Feed-forward SPN activity might regulate the functional maturation and plasticity of A1 and contribute to the development of normal cortical organization.

Envelope Representation in Background Noise by Auditory Cortex Neurons

Yi Zhou, Xiaoqin Wang

Laboratory of Auditory Neurophysiology, Dept of Biomedical Engineering, Johns Hopkins Univ., Baltimore, MD

In a noisy listening environment, sound perception is limited but does not necessarily fail. One hypothesis is that the amplitude envelope of a sound provides an important temporal cue for its detection in noise. Previous tone-in-noise experiments in auditory cortex have shown that background noise results in a threshold shift and a steeper slope in rate-level tuning. It remains unclear, however, what happens to the spike timing of cortical responses in the presence of noise when a dynamic sound is heard. We examined in the present study the neural representation of envelope contours in the presence of broad-band noises in the auditory cortex of awake marmosets. Slow (<10 Hz)

aperiodically amplitude-modulated tones (centered at a unit's characteristic frequency, CF) were used as the foreground stimuli. In both the presence and absence of noise, we found that cortical responses were locked to the peak of stimulus contour when the stimulus amplitude was weaker than the peak of the rate-level function measured by a CF-tone, but locked to the slope of stimulus contour when the stimulus amplitude was stronger than the peak of the rate-level function. However, adding background noise often altered temporal discharge patterns of the envelope-locked responses (for example, broadening, sharpening or abolishing the envelope-locking). These results were directly correlated with changes in sound-level tuning of a neuron in the presence of background noise. Similar to previous findings in anesthetized auditory cortex, we observed that noise can suppress neural responses to tones, especially at high noise levels. In addition, we found that noise can also increase responses of a neuron long after the onset of noise, suggesting that the interaction between excitatory and inhibitory processes elicited by tone-in-noise stimuli underwent a longer time scale in the awake condition. >From a signal detection point of view, the reduced perceptual saliency of a signal in noise may result from reduced or altered temporal fluctuations in neural firing patterns due to the presence of noise. Alternatively, noise could have an enhancing effect on signal detection by strengthening temporal response patterns (a phenomenon known as the stochastic resonance). An envelope-locking response in noise may manifest a robust neural representation that is tolerant to interruption and thus enables transmitting information in a noisy acoustic environment. [Supported by NIH Grant R01-DC003180 (X.W.)]

Behavioral and neural discrimination of temporally asymmetric sounds in cats

Y. SATO, J. WANG, SN. LI, L. QIN;

Dept Physiol, Univ. Yamanashi, Chuo, Japan

Sound wave envelope plays a crucial role for sound discrimination. For example, human subjects discriminate temporally asymmetric envelopes with identical spectra. We investigated such capability in cats by using damped and ramped sinusoids as stimuli for the go/no go task. The cats were trained to discriminate 160-ms duration of damped/ramped sinusoids (4 kHz, 50 dB SPL). After the cat's performance reached the criterion level ($d' = 2$) and remained higher than it for 5 continuous sessions (100 trials per session), we tested the duration dependence of the discrimination in the following 5 sessions (duration: 80, 40, 20, 10, and 5ms). The discrimination capability obtained from the training of 160ms tones was immediately transferred to the tones more than 40 ms ($d' > 2$), which were novel sounds for the subjects, but not to the tones less than 20ms ($d' < 2$). Next, we repeated the training and test procedures to other carrier frequencies of 2, 8, 16 kHz and intensities of 35, 65dB SPL, and found similar results. Finally, cats were successfully trained to discriminate short-duration damped/ramped tones of 10, 5 ms ($d' > 2$), suggesting that the cats may use differential cues between the short and long tones. To investigate underlying neural mechanism, we recorded the single-unit spike activities from the primary auditory cortex (A1) of naïve awake cats passively listening to the stimuli. For the durations

longer than 40ms, all the recorded cells showed different response time courses to the asymmetric stimuli. The cells showed sustained response time courses mimicking the damped and ramped stimulus envelopes, respectively; or showed salient offset responses to the ramped sounds, but not to the damped sounds. For the short stimuli less than 20ms, the mean response time course averaged over the cell population exhibited a similar transient single-peak for both the damped and ramped stimuli. However, the peak amplitude of individual responses showed a damped or ramped preference in about 2/3 cells. These duration-dependent neural response features may explain the duration-dependent behavioral performance of asymmetry discrimination. *This work was supported by Grant-in-Aid for Scientific Research B (No.20300076) from Japan Society for the Promotion of Science (JSPS), and National Nature Science Foundation of China under Grant (No.30700938)*