C125

Decreased ankle joint eversion prior to and following initial ground contact during hopping in individuals with chronic ankle instability (CAI)

E. Delahunt, K. Monaghan and B. Caulfield

School of Physiotherapy, University College Dublin, Dublin

Introduction:
CAI, a subjective feeling of ankle instability or, recurrent symptomatic ankle sprains (or both), is the most serious residual disability following ankle sprains. To date, there have been no thorough investigations into the 3D kinematic patterns of subjects with CAI prior to and following initial ground contact during hopping. The purpose of this study was to undertake a comprehensive analysis, of the 3D kinematic patterns associated with hopping in a group of subjects with CAI, with the aim of determining whether changes in the neural control of movement and dynamic stability of the ankle joint exist in the these subjects.
Methods:
Thirteen subjects with unilateral CAI and 16 control subjects volunteered to participate. Inclusion criteria in the CAI group were based on the criteria used by Caulfield and Garrett (2004). CODA mpx 30 (Charnwood Dynamics Ltd.) infrared light emitting diodes were attached to the involved lower extremity in the CAI group and the left lower extremity in the control group and were used to provide information pertaining to 3D segment angular displacement and angular velocity. Subjects performed 10 single leg lateral hops onto a force platform from a distance of 30cm from the edge of the force platform.
Average values for hip, knee and ankle joint 3D angular displacements and velocities were calculated for each subject. Group mean time averaged profiles (200ms pre initial contact (IC) to 200ms post initial contact) were calculated. Differences in CAI and control group time averaged profiles were tested for statistical significance using independent two-sided t-tests.
Results and Discussion:
CAI subjects exhibited a significant decrease in ankle joint eversion during the time period 10ms pre IC to 200ms post IC ($p<0.05$). A less everted position of the ankle joint will cause the subtalar joint axis to remain in a more lateral position. Consequently a greater external inversion load could be placed upon the ankle joint, thus increasing the potential for a hyperinversion injury.
Conclusion:
The disordered positioning of the ankle joint observed in subjects with CAI, manifests prior to and immediately following initial contact with the ground, rendering reflex correction impossible. Consequently this may result in repeated injury to the chronically unstable ankle, as a result of the potentially injurious external inversion load created by a less everted position of the ankle joint following initial ground contact.

Caulfield, B. & Garrett, M. (2004). Clin Bimech 19, 617-621.

This study was supported by the Irish Research Council for Science, Engineering and Technology.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C126

Fast adaptation and hair bundle mechanics in rat outer hair cells

H. Kennedy[1], A. Crawford[2] and R. Fettiplace[3]

[1]Physiology, University of Bristol, Bristol, UK, [2]Physiology, University of Cambridge, Cambridge, UK and [3]Physiology, University of Wisconsin, Madison, WI, USA

The properties of the mechanotransducer (MET) channels and how they influence the mechanical properties of the hair bundle have been amply documented in hair cells of lower vertebrates. In the turtle, transduction exhibits a fast adaptation with a time constant varying inversely with the hair cell characteristic frequency (CF) (Ricci *et al.*, 2003). Fast adaptation reflects calcium-dependent reclosure of the MET channels, which can in turn elicit a mechanical reaction that moves the hair bundle. To ascertain whether measurements in the turtle provide a good paradigm for mammals, we have studied the properties of hair cell MET currents in mammalian outer hair cells. Currents were recorded at room temperature 19-22°C from hair cells in acutely isolated cochleae of humanely killed rats between postnatal days 6 and 12. The tectorial membrane was removed and the upper surface of the hair cell epithelium was separately perfused through a 100 μm pipette with a saline containing (2.8 mM) or endolymph-like (0.05 mM) $CaCl_2$. Hair bundles were deflected with a glass pipette driven by a high-speed piezoelectric actuator, and currents were measured under whole-cell voltage clamp (Kennedy *et al.*, 2003). In response to a step displacement of the hair bundle, MET currents activated with a time course indistinguishable from the mechanical stimulus, but then adapted with a time constant of less than 0.1 ms. As in turtle, both the size and adaptation rate of the MET current depended on external calcium concentration. Comparison of two cochlear locations with CFs of 4 and 14 kHz showed that cells with higher CF had on average larger MET currents and faster adaptation to those with low CF. At high CF and 2.8 mM external calcium adaptation time constants as fast as 50μs were recorded. At more physiological calcium levels of 0.5mM the time constant was reversibly slowed to 90 μs, but the speed with which the MET current developed was too fast to measure, even at room temperature. Fast activation and adaptation kinetics are consistent with the higher frequencies encoded by the rat cochlea. We also examined the mechanical properties of outer hair cell bundles using force?stimulation with flexible fibers whose motion was determined by imaging on a dual photodiode. The force-displacement relationship of the hair bundle was non-linear over the range where the MET channels were gated and in some cells showed evidence of a negative slope region similar to that observed in frog saccular hair cells. Such non-linearity was sensitive to external calcium and developed with a time course similar to fast adaptation (Kennedy *et al.*, 2005). We conclude that fast adaptation in outer hair cells functions on a time scale appropriate for cycle-by-cycle regulation at the hair cell CF, and we suggest it is linked to force generation the hair bundle that may contribute to the cochlear amplifier.

Ricci AJ *et al.* (2003). *Neuron* **40**, 483-490.

Kennedy HJ *et al.* (2003). *Nat Neurosci* **6**, 832-836.

Kennedy HJ *et al.* (2005). *Nature* **433**, 880-883.

Supported by NIH grant RO1-DC01362 to RF.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C127

'What' and 'where' in the auditory system – 'where' and 'when' in the human brain?

I. Anurova[1], D. Artchakov[1], A. Korvenoja[2], R. Ilmoniemi[3], H. Aronen[4] and S. Carlson[1]

[1]Inst. Biomed./Physiology, University of Helsinki, Helsinki, Finland, [2]Dep. Radiology, Helsinki University Central Hospital, Helsinki, Finland, [3]Nexstim Ltd., Helsinki, Finland and [4]Cognitive Brain Res. Unit, University of Helsinki, Helsinki, Finland

The present research project was focused on neuronal mechanisms underlying the processing of sound content and its spatial location. In recent years, the idea of segregation of spatial and non-spatial auditory processing into separate pathways has gained support from psychophysical (Clarke et al. 1998), electrophysiological (Alain et al. 2001; Anourova et al. 2001) and neuroimaging studies (Alain et al. 2001; Warren & Griffiths, 2003). Results from our earlier experiments (Anourova et al. 2001, 2003) suggest that the dissociation between spatial and non-spatial auditory information processing occurs within the supratemporal plane as early as at about 100 ms from stimulus onset. In the present study we employed the whole-head electro- and magnetoencephalographic recordings in order to investigate the spatiotemporal dynamics during location and pitch auditory information processing in the higher-order associative areas. We analyzed slow evoked responses (the P3 and positive slow wave (PSW), the prominent positive deflection following the P3) elicited by probe stimuli in location and pitch working memory tasks. The number of successive trials averaged for each experimental condition (match and non-match, either location or pitch) was about 200. Minimum current estimates suggested that associative temporal areas in the posterior and middle parts of the superior temporal sulcus were sensitive to sound attribute. The occipito-temporal generator of the P3 was activated more during the spatial than nonspatial task, and the left temporal generator of the PSW tended to be more strongly activated during the non-spatial task. Furthermore, analysis of the source coordinates (2-way ANOVA) revealed a structural segregation in the location of the center of active area within the occipito-temporal cortex: in the location task, the right-hemispheric occipito-temporal source was situated significantly more medially than in the pitch task ($p < 0.05$). These findings provide evidence for segregation of spatial and non-spatial auditory information processing in associative areas beyond the supratemporal auditory cortex and support the dual-stream model for auditory information processing.

Alain C et al. (2001). Proc Natl Acad Sci USA 98, 12301-12306.

Anourova I et al. (2001). NeuroImage 14, 1268-1277.

Anurova I et al. (2003). NeuroImage 20, 1181-1192.

Clarke S et al. (1998). NeuroReport 9, 3433-3437.

Warren JD & Griffiths TD (2003). J Neurosci 23, 5799-5804.

This study was supported by The Academy of Finland and Sigrid Juselius Foundation.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C128

Interocular cross-orientation suppression in cat striate cortex involves intracortical inhibition

F. Sengpiel and V. Vorobyov

School of Biosciences, Cardiff University, Cardiff, UK

Cross-orientation suppression (COS) in V1 is commonly thought to result from intracortical inhibition. This hypothesis was rejected by Freeman et al. (2002), who suggested an origin in the LGN. We examined the nature of COS elicited by dichoptically presented gratings in V1 of anaesthetized neuromuscularly blocked cats, employing single-cell recordings.

Details of animal preparation have been described elsewhere (Sengpiel et al. 1995). Briefly, anaesthesia was induced with an i.m. injection of ketamine (20-40 mg/kg) and xylazine (2-4 mg/kg). Following tracheal cannulation, animals were artificially ventilated and anaesthetized with a mixture of N2O (55-65%), O2 (35-45%) and isoflurane (2-2.5% during surgery, 1-1.5% during recording). During recording the animal was neuromuscularly blocked with a continuous i.v. infusion of gallamine triethiodide (10 mg/kg/h) in glucose-saline. E.C.G. and E.E.G. were constantly recorded to monitor the state of anaesthesia. Animals were killed with an overdose of barbiturate at the end of the experiment.

First, we studied the dependence of COS on the drift rate of the suppressing grating. Temporal frequency tuning of monocular cross-orientation suppression was recorded in 73 neurons, interocular suppression in 74 cells. Of those, 46 neurons were tested under both suppression paradigms. Overall, the tuning of interocular suppression closely matched the tuning of the cells' excitatory responses, with cut-off rates of 8-16 Hz. In contrast, monocular COS was observed for drift rates of up to 32 Hz, similar to LGN responses.

Second, we tested whether interocular COS was affected by adaptation to the suppressor. If COS were of geniculate origin, adaptation to the suppressor should not affect its strength, since firing rates in the LGN decrease only slightly. We measured contrast-response functions in the presence and absence of a suppressing grating and found that mean interocular COS was reduced from 33.4% ± 2.9% (mean ± SEM) without prior adaptation to 5.6% ± 8.7% after adaptation to the masking grating. Suppression under these two conditions differed significantly ($p < 0.001$, paired t-test).

Third, we locally antagonized intracortical inhibition by bicuculline micro-iontophoresis and found that interocular COS was reduced from 46.1% ± 4.0% (mean ± SEM) prior to application of bicuculline to 18.1% ± 4.9% during application of bicuculline. Suppression under these two conditions differed significantly ($p < 0.001$, paired t test).

Taken together, our data demonstrate that interocular COS is substantially different from monocular COS and that it is mediated by inhibitory circuitry within the visual cortex.

Freeman TC, Durand S, Kiper DC & Carandini M (2002). Neuron 35, 759-771.

Sengpiel F, Blakemore C & Harrad R (1995). Vision Research 35, 179-195.

This work was supported by the Medical Research Council (UK) and the Human Frontier Science Program.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C129

Cortical representation and lateralization of taste in man

M. Fabri[1], G. Polonara[2], G. Mascioli[2], G. Tassinari[3], G. Berlucchi[3], S. Aglioti[4], U. Salvolini[2] and T. Manzoni[1]

[1]Dipartimento di Neuroscienze - Sezione di Fisiologia, Universita'Politecnica delle Marche, Ancona, Italy, [2]Dipartimento di Neuroradiologia, Universita' Politecnica delle Marche, Ancona, Italy, [3]Dipartimento di Scienze Neurologiche e della Visione, Universita'di Verona, Verona, Italy and [4]Dipartimento di Psicologia, Universita'di Roma "La Sapienza", Roma, Italy

In the human brain taste is represented in the primary gustatory area (GI), a cortical region lying at the transition between the frontoparietal operculum and the insula. This notion has been repeatedly confirmed with MEG, PET and fMRI studies. The latera lization of taste representation, i.e. whether unilateral taste stimuli activate the contralateral or ipsilateral GI, or both areas, is still a controversial issue.

The present research was aimed at establishing whether the cortical representation of taste in area GI is mainly ipsilateral as in non-human primates, or bilateral, as suggested by recent neuropsychological studies of patients with callosal resection or cerebral lesions.

Six neurologically intact subjects gave their informed consent to participate in the study according to a protocol approved by the Local Ethical Committee and in accord with the Declaration of Helsinki. Functional images were acquired by using a General Electric Signa CV/i-NV/I, with a 1.5 Tesla magnet and 50 mT/M gradients in the three spatial directions. The images of 10 contiguous 5-mm-thick encephalic sections parallel to the axial plane were acquired with an echoplanar sequence. Gustatory stimulation was performed by placing a small cotton pad soaked in 1M NaCl solution on the side of either hemitongue. The stimulation protocol lasted 5 min and consisted of 60 s rest, 30 s stimulation, 90 s rest, 30 s stimulation, 90 s rest. Data were analysed with BrainVoyager and SPM2 software. A statistical value of $P < 0.05$ was considered to show significant activation.

Preliminary results indicate that salty stimulation of the left hemitongue l ed to a clear-cut activation of area GI in the left hemisphere (mean Talairach coordinates: x, -37; y, 21; z, 1) in all subjects, coupled with an activation of the right GI (x, 37; y, 23; z, 5) in 4 of them. Stimulation of the right hemitongue caused a bi lat eral activation of GI (mean Talairach coordinates: right x, 39; y, 14; z, 1; left x, -43; y, 13; z, 0) in 4 subjects, while GI activation was ipsilateral to the stimulus in one of the 2 remaining subjects and contralateral in the other one.

The results s uggest that in most neurally intact subjects unilateral taste stimulation evokes bilateral activation of area GI. They are generally compatible with our previous findings in callosotomy patients (Aglioti et al. 2001), according to which 'gustatory pathways from tongue to cortex are bilaterally distributed, with an ipsilateral predominance that may be subject to individual variations'.

Aglioti SM et al. (2001). Eur J Neurosci 13, 195-200.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

PC209

Fast and slow responses to acetylcholine in outer hair cells

P. Darbon, D.J. Wright and M.G. Evans

MacKay Institute of Communication and Neuroscience, Keele University, Newcastle-under-Lyme, UK

Outer hair cells (OHCs) of the mammalian cochlea have a nicotinic acetylcholine receptor (AChR) comprising α9 and α10 subunits and forming a cation channel with a high calcium permeability (see Lioudyno et al. 2004). Acetylcholine produces inhibition of OHCs as calcium influx through this receptor gates a SK-type calcium activated potassium current. Experiments on isolated OHCs showed that the response was rapid, activating in 200 ms (Evans, 1996). We have observed a slow current in OHCs that appears to flow through the same AChR.

Guinea pigs were humanely killed and OHCs isolated from cochlear turns 2 and 3 as described previously (Evans, 1996). Whole-cell voltage-clamp recordings were made from OHCs at room temperature. ACh (100μM) was pressure-applied from a pipette positioned about 20 μm from the cell base. The pipette (internal) solutions were KCl/5 mM EGTA (see Evans, 1996) or CsCl/10 mM BAPTA, the latter being used to monitor the AChR current in isolation.

With the CsCl/BAPTA solution, I-V plots of the AChR current had a reversal potential of -4 mV and prominent rectification, particularly in the outward direction. The current activated in 150 ms. With the KCl/EGTA solution, the ACh-evoked current usually had an N-shaped I-V relation as expected for a calcium activated potassium current dependent on calcium influx. Occasionally ACh application produced a much slower current, activating over about 1 s after a 0.5 s delay, either on its own or in addition to the faster potassium current. This current was similar to the AChR current in terms of reversal potential and block by α-bungarotoxin (0.4 μM), but was larger (up to -1 nA at -60 mV) and inwardly rectifying. It was still present in low external calcium (0-0.4 mM) and was more commonly observed under these conditions (in ~50% of recordings compared to ~5% in controls). Application of ACh during exposure (4 min) to external thapsigargin (1-5 μM) or 2,5-di-(t-butyl)hydroquinone (BHQ, 50 μM) did not produce the slow current, suggesting that calcium stores are not involved. This current appears to be a slower kinetic version of the fast AChR current.

Evans MG (1996). J Physiol 491, 563-578.

Lioudyno M et al. (2004). J Neurosci 24, 11160-11164.

This work was supported by The Wellcome Trust and British Tinnitus Association.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

PC210

Processing of spatial properties of auditory and visual stimuli in the monkey prefrontal cortex

D. Artchakov[1], I. Linnankoski[1], D. Tikhonravov[1], V. Vuontela[1], A. Korvenoja[2] and S. Carlson[1]

[1]Inst. Biomedicine/Physiology, University of Helsinki, Helsinki, Finland and [2]Functional Brain Imaging Unit, Medical Imaging Center, Helsinki University Central Hospital, Helsinki, Finland

The primate dorsolateral prefrontal cortex (PFCd) is involved in visuospatial (1,2,3) and audiospatial (4) working memory. Visuospatial working memory mechanisms have been studied extensively at single cell level in the PFCd in nonhuman primates but, despite the importance of short-term memory of sound location for behavioral orientation, there are only a few studies (4) on working memory processing of auditory location. The purpose of this study was to investigate neuronal mechanisms underlying working memory processing of auditory and visual location information and possible interactions between these modalities at single cell level in the PFCd. Neuronal activity was recorded in two monkeys (Macaca mulatta) trained to perform audio- and visuospatial delayed matching to sample tasks, that required them to memorize and compare the locations (left or right) of the visual or auditory cues. For the surgery the monkeys were anaesthetized (ketamine hydrochloride 4 mg/kg i.m., pentobarbital sodium 18 mg/kg i.v.). The tasks enabled separation between neuronal activity related to encoding and maintenance of sensory information and movement preparation. A total of 325 neurons were recorded during both visual and auditory task performance. Of the neurons 287 were from the right and 38 from the left hemisphere. The activity of 111 neurons (34%) was related to some phase (cue, delay, response or reward) of the task. Twenty neurons responded during more than one phase of the task. Visually responsive, auditory responsive, and bimodal spatial neurons were found within the recorded region in the PFCd (Table 1). Of the spatially selective neurons, all delay related and most cue related neurons were modality specific and responded either during auditory or visual trials. A small number of cue related neurons were bimodal and displayed similar selectivity for spatial locations in both sensory modalities. The results indicate that processing of auditory and visual spatial information during encoding and memory maintenance involves mainly parallel cellular mechanisms, but the data also imply the existence of crossmodal mechanisms of working memory processing of auditory and visual location information in the PFCd. The maintenance of the monkeys and all procedures of the study were carried out according to the Finnish law and statutes governing animal experimentation. The Finnish Ministry of Agriculture had approved of the study and granted permission to perform it.

Table 1. Spatial selectivity of cue- and delay-related visual, auditory and bimodal neurons

		Visual	Auditory	Bimodal	All
Spatially selective	Cue	23	7	4	34
	Delay	6	2	-	8
Spatially non-selective	Cue	10	3	1	14
	Delay	5	1	2	8

Goldman-Rakic PS (1995). Neuron 14, 477-485.

Funahashi S et al. (1989). J Neurophysiol 61, 331-349.

Fuster JM (1997). The Prefrontal Cortex, 3rd edn. Lippincott-Raven, Philadelphia.

Kikuchi-Yorioka Y & Sawaguchi T (2000). Nat Neurosci 3, 1075-1076.

The study was supported by grants from the Academy of Finland (179821, 1201955, 174112), Centre for International Mobility, Helsinki University Central Hospital and EU 5th framework programme contract QLK3-CT-1999-00894.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.