SA01

Sensory neuron mechanotransduction, mechanisms and molecules

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Somatic sensation is overwhelmingly felt as the result of mechanical stimulation or movement of the body or its parts. Indeed almost all tissues of the body receive an innervation from the peripheral axons of mechanosensitive sensory neurons with their cell body in the dorsal root or trigeminal ganglia. Remarkably, the mechanisms and molecules used by sensory neurons to transform mechanical force into an electrical signal are poorly understood. We term this process sensory neuron mechanotransduction, to distinguish it from mechanotransduction in the specialized epithelial hair cells of the inner ear. It is assumed that specialized mechanosensitive ion channels that are gated by force, underlie a graded receptor potential in sensory afferent endings. The graded receptor potential leads to action potential firing that decodes the stimulus magnitude. We have sought to be able to measure mechanosensitive currents in isolated sensory neurons in acute culture that presumably underpin the receptor potential. We have found two main types of highly sensitive mechanosensitive currents in the neurites and somas of sensory neurons (Hu and Lewin, 2006; Lechner et al. 2009). These two currents have been termed rapidly-adapting and slowly adapting mechanosensitive currents. The rapidly adapting (RA-type current) is found in all mechanoreceptors but also in a substantial number of nociceptors and this current inactivates very rapidly. The slowly adapting current (SA-type) has a distinct pharmacology and biophysical profile from the RA-type current and is only found in nociceptive sensory neurons. The relevance of mechanosensitive currents for in vivo mechanosensitivity has been demonstrated by experiments showing that such currents are absent in neurons with a targeted disruption of the gene encoding the integral membrane protein called stomatin-like protein-3 (SLP3) (Wetzel et al, 2007). In SLP3 mutant mice a substantial number of sensory afferents in the skin completely lack mechanosensitivity. Recently we have addressed the mechanism by which the mechanosensitive current is activated in sensory neurons. In principle the current could be activated by membrane stretch or, analogous to the hair cell, an extracellular tether might transfer force from the matrix directly to the channel. We have used a variety of tools to manipulate extracellular proteins including limited proteolysis and combined physiological measurements with quantitative transmission electron microscopy. These experiments show that the presence of an extracellular tether protein filament with a length of 100 nm appears to be necessary for gating the RA-type current. The tether molecule is synthesized by sensory neurons and binds to a laminin-containing matrix. Our data is the first to show that a tether gating mechanism is relevant for somatic sensory neurons. Interestingly, activation of the SA-type current does not appear to depend on a link to the extracellular matrix.

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SA02

Detecting Sound: Mechano-electrical transduction in the ear

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Auditory hair cells are specialized epithelial cells that are able to detect sound vibrations and convert them into electrical signals. The mammalian cochlear contains two classes of sensory hair cells that have distinct functions. Inner hair cells are responsible for detecting and encoding sound stimuli. Outer hair cells are thought to boost quiet stimuli by an electromechanical feedback process termed the 'cochlear amplifier' that increases sensitivity and frequency selectivity of our hearing.

Mechanical vibrations are detected by the hair bundle that sits at the hair cell apex. In outer hair cells, mechanical displacement of the hair bundle with stiff glass fibers elicits a fast activating transducer current. The activation rate of the channel is too fast for us to measure; even at room temperature. In the presence of a maintained deflection the transducer current adapts with a very rapid time course, in the order of 100 μs (Kennedy et al., 2003). This rate of adaptation and the size of the transducer currents are dependent on the characteristic frequency of the cells, with high frequency cells showing much larger and faster adapting currents than low frequency cells (Ricci et al., 2005). In contrast, inner hair cells show slower adaptation time constants and the size and adaptation rate of the currents are not frequency dependent, but are uniform along the length of the cochlear (Beurg et al., 2006). These differences may reflect the different functions that inner and outer hair cells serve.

Outer hair cells are thought to underlie the cochlear amplifier, and until recently, the only mechanism proposed in mammalian systems was mechanical force generation through cell length changes. This somatic motility is thought to be driven by receptor potential changes that drive conformational changes in the membrane protein Prestin. However, questions still remain about how Prestin would be driven at high frequencies when receptor potentials would be expected to be attenuated by the membrane time constant. In non mammalian systems amplification is achieved by the hair bundle. Force is thought to be generated by the mechano-transducer channel itself, which, unlike somatic motility, would not be limited by the membrane time constant of the cell. Experiments using flexible glass fibers have shown that outer hair cell bundles in mammalian hair cells are also capable of force generation, and that the rate of this force generation closely matches fast adaptation rates (Kennedy

et al., 2005). As the rate of adaptation varies with characteristic frequency, so could force generation. In addition, as in non mammalian systems this mechanism would not be limited by the membrane time constant, making it an attractive candidate for the cochlear amplifier. However, questions still remain as to whether and how somatic motility or hair bundle force generation might underlie cochlear amplification. This presentation will summarize recent advances in our understanding of mechano-transduction in mammalian hair cells.

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SA03

The dominant time constant for light response recovery has different origins in rod and cone photoreceptors

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Transduction in vertebrate photoreceptors takes place via an enzymatic cascade in which photoisomerised photopigment acts via a G-protein, transducin, to activate a phosphodiesterase enzyme which hydrolyses cGMP, leading to the closure of cyclic nucleotide-gated channels in the outer segment membrane and the electrical response to light. The time constant which dominates light response recovery is set by the slowest of the steps that quench the phototransduction cascade. Candidates for this dominant time constant comprise either the shutoff of photopigment catalytic activity or shutoff of the activated transducin-phosphodiesterase complex. This distinction is functionally important, since photopigment quenching, but not transducin shutoff, is known to be modulated by the decline in Ca^{2+} concentration which takes place during the light response. In rod photoreceptors, the dominant time constant for response recovery is not affected by Ca^{2+}, thereby excluding rhodopsin quenching. Instead, it has been shown to depend on the GTPase activity of transducin, which therefore dominates response recovery. However, in cones of all colour classes the time constant that dominates response recovery depends strongly on Ca^{2+}, and can be modulated by manipulations that are known to affect photopigment quenching. These observations indicate that in cones, unlike rods, photopigment quenching dominates response recovery and provides an additional mechanism for adaptation of the cone response during steady light.

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SA04

Functional expression of mammalian odorant receptors

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Our ability to smell relies on odorant receptors (ORs) in the olfactory sensory neurons of the olfactory epithelium. Mammalian ORs are seven transmembrane G-protein-coupled receptors that are expressed on the cilia membrane at the tip of the dendrite in the olfactory sensory neurons. Each OR is specialized to bind specific features of odorant molecules. ORs represent the largest gene superfamily in the mammalian genome and account for the diversity of odors that we can detect, yet it is not known how the olfactory system encodes an olfactory percept. Understanding how a range of perceptual qualities regarding tens of thousands of odorants interacting with hundreds of ORs requires an assay that can probe a large number of single odorant-single receptor interactions. Heterologous expression systems allow us to probe the interaction of a single odorant with a single receptor. The discovery of chaperone proteins, RTP1 and RTP2, that enhance the cell-surface expression of ORs allowed us to develop a high throughput screening system for ORs. By describing the large number of OR-ligand interactions, we hope to be able to relate properties of odorants and the ORs.

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SA05

The postnatal development and plasticity of spinal and brainstem inhibitory pain controls

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The postnatal period is a critical time for developing pain pathways. Over the first weeks of life nociceptive circuits are shaped, endogenous pain control systems are activated and pain behaviour is organised (Fitzgerald, 2005). As in other sensory systems, these processes are strongly influenced by sensory experience and as such could be viewed as a form of learning. For the pain system, this creates a special vulnerability. Repeated peripheral tissue damage, such as arises in neonatal intensive care or surgery, alters the physiological balance of sensory input and changes the course of somatosensory development, pain perception and behaviour. We propose that the key to the plasticity of immature nociceptive circuits lies in the late postnatal maturation of endogeous pain control systems within the CNS. This presentation therefore focuses upon our recent data on the maturation of inhibitory controls over the postnatal period.

In adults, pain perception and behaviour is powerfully controlled at the level of the spinal cord by local inhibitory circuits and by descending activity from brainstem nuclei. An important source of spinal pain modulation comes from dorsal horn glycinergic inhibitory interneurons which can powerfully control evoked spike activity and regulate dorsal horn cell receptive field size. This local inhibition is recruited by the afferent input itself and in adults, its failure can lead to acute and chronic pain (Zeilhofer and Zeilhofer, 2008). We have previously shown that dorsal horn inhibitory processing undergoes considerable postnatal maturation at the synaptic (Ingram et al. 2008) and circuit (Bremner and Fitzgerald, 2008) level. In addition there are little or no glycinergic PSCs in neonatal lamina II cells and inhibitory neurotransmission in lamina II of the dorsal horn is dominated by GABAergic transmission in the early stages of development (Baccei et al. 2005). Here we will present new data on the role of glycine on deep dorsal horn cell activity and receptive fields over postnatal development and the influence of the maturation of spinal glycinergic inhibition upon neonatal pain processing.

Nociception and pain behaviour is also powerfully controlled at the level of the spinal cord by descending activity from brainstem nuclei, particularly the rostroventral medulla (RVM) and periaqueductal grey (PAG). In the adult, a background, descending tonic inhibition normally dampens acute nociceptive input but this can shift to facilitation under conditions of persistent or chronic pain (Heinricher and Lumb, 2008). This brainstem axis is the major site of action of the analgesic actions of opioids. We have recently discovered that the descending RVM control of spinal sensory circuits undergoes a remarkable maturational switch over postnatal development (Hathway et al. 2009). Both lesioning and electrical stimulation of RVM at different postnatal ages reveal that RVM control switches from being entirely facilitatory before 3 weeks of age to predominantly inhibitory by 4 weeks. The effect is observed upon both spinal nociceptive reflexes and dorsal horn neuronal activity over this critical developmental period and is likely to be of considerable importance for the maturation sensory transmission and integration. Here we will present new data that establishes a critical period for this switch in descending control and shows that endogenous opioid activity is essential for its normal maturation.

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SA06

Cortico-thalamic interactions in perceptual processing

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In the central visual system feedback interactions parallel the feed forward connections and there are arguments for considering its function in terms of iterative interactions in a circuit rather than a sequence of processing steps. From this viewpoint it is notable that in the primate visual system the cortical motion area MT/V5 provides feedback to the primary visual cortex (V1) with the potential to provide cascaded feedback to thalamic relay cells in the LGN (Born & Bradley 2005, Sillito *et al.* 2006, Briggs & Usrey 2009). Feedback from MT to V1 exerts strong and clear effects on V1 responses to flashing and moving stimuli. A component of feedback connections from MT to V1 terminate in upper and lower layer 6 where cortico-geniculate neurons providing feedback to the magno and parvo cellular layers of the LGN are found. Layer 6 cells in V1 influence the visual responses and response pattern of LGN cells. This has the surprising implication that information about stimulus motion and direction reflected in the responses of MT cells is available to LGN cells. Is it?

To date there is no evidence to suggest that LGN cell visual response properties resemble those of MT cells. However this might reflect the fact that cascaded feedback from MT direction columns is pooled so that for any given point in visual space a complete set of direction columns influences the responses of LGN cells, in effect averaging out any directional bias. To isolate possible influences from MT we explored the effect of blocking the activity of a locus in the columnar organization of MT representing a particular direction of motion with a brief iontophoretic pulse of GABA. We predicted that if feedback from MT influenced LGN cell responses blocking the MT locus would cause changes in the responses of LGN cells biased to that direction of motion.

We recorded from 133 primate LGN cells (*Macaca mulatta*, anesthetized with sufentanil 4μg/kg/hr supplemented with halothane (0.1-0.4%) in 70% N_2O/30% O_2. Neuromuscular blockade was induced with 0.1mg/kg/hr vecuronium bromide and anaesthesia monitored as previously described (Jones *et al.* 2001) during reversible blockade of an MT direction column. Of these LGN cells, 96 showed a reversible and significant shift ($P < 0.05$ paired two tailed T test) in directional bias during the focal blockade of MT. There was a significant difference between LGN cell control firing rate to stimuli moving in the preferred direction of the MT column and those observed when the activity of the MT column was blocked by drug application ($P = 0.023450$ Wilcoxon matched pairs test) but not between firing rates for control and drug conditions when the stimulus was moving in the non preferred direction. We checked whether there was variation in the effect of MT inactivation across the

three types of LGN cells. The geometric mean of the change in directional bias was 43.9% for magnocellular cells (n = 24, 95% CI 37.07, 51.89), 19.8% for parvocellular cells (n = 92, 95% CI 15.15, 25.90) and 6.3% for konicellular cells (n = 17, 95% CI 2.75, 14.50). These values across the three cell classes were significantly different to each other (P = 0.0000, Kruskal-Wallis Anova). We checked if the magnitude of effect was influenced by whether the LGN fields overlapped with the MT field or not. For parvocellular cells there was a significant variation (P = 0.000002 Mann Whitney U test) in effect if the LGN receptive field overlapped the MT field or not, with geometric mean values for overlapping cells of 9.9% (n = 34, 95% CI 6.19, 15.71) and non overlapping cells of 29.8% (n = 58, 95% CI 22.40, 39.69). The difference in values for overlapping and non-overlapping koni and magnocellular cells were not significant. We also observed larger effects in magno and parvocellular cells if their receptive fields lay close to the angular vector defining the preferred direction of motion of the MT column inactivated.
Basically our observations reveal a constant stimulus driven background modulation of LGN cell responses by feedback from MT. This introduces the context of salient motion integrated over a much wider area than the subcortical process in isolation. In the sense that these changes in LGN cells responses will provoke a change in the input to V1, and thus a change in the input to MT and a consequential change in MT responses and its feedback back to V1 and the LGN, our data argue for a constant reiterative mechanism locking onto the stimulus. From this perspective the representation of the stimulus sits in the interaction between the levels.

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SA07

Transformation in ITD coding in the auditory midbrain

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For many species, the ability to encode the location of a sound source relies on comparing differences in the phase of the acoustic waveform arriving at each eardrum (the interaural time difference, ITD). This comparison takes place three synaptic stages beyond the sensory epithelium of the inner ear, requiring extraordinary, and well-documented, neural mechanisms to ensure fidelity of the signal to this point. Following this stage of processing, a significant transformation in neural coding of ITD occurs in the auditory midbrain, rendering neurons sensitive not only to the instantaneous ITD, but also the longer-term context in which ITDs were presented. Using a combination of single-neuron recordings and modeling, we demonstrate that at the level of midbrain neurons, this sensitivity requires the action of both brain hemispheres and a range of neural time-constants, implemented variously through circuits implementing fast (iontotropic) and slow (inhibitory metabotropic) neurotransmitters. Psychophysical experiments support the notion that the context in which ITDs are heard influences performance in a discrimination task in which noise bursts containing ITDs are made more discriminable by appropriate (i.e. co-located) preceding sounds hypothesis, an observation that accords with the efficient coding hypothesis.

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SA08

Dynamics of population responses in visual cortex

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The perception of visual stimuli is widely held to be supported through the activity of populations of neurons in visual cortex. Work in our laboratory seeks to record this population activity and to characterize its evolution in time. Our methods rely on optical imaging of voltage-sensitive dyes (Benucci et al, 2007) and on electrical imaging via multielectrode arrays (Nauhaus et al, 2009).
Our results indicate that the visual cortex operates in a regime that depends on the strength of the visual stimulus: For large, high contrast stimuli, the cortex operates in a manner that emphasizes local computations, whereas for smaller or lower contrast stimuli the effect of lateral connections becomes predominant. In this interconnected regime, the population responses exhibit rich dynamics, with waves of activity that travel over 2-6 millimetres of cortex to influence distal locations. In the complete absence of a stimulus, these waves dominate, and are sufficient to explain the apparently erratic activity of local populations. These results indicate that two apparently contradictory views of visual cortex, one postulating computations that are entirely local and the other postulating strong lateral connectivity, are both correct. The cortex can operate in both regimes, and makes its choice of regime adaptively, based on the stimulus conditions.

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SA09

Information Processing in the Auditory Cortex

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Compared to other sensory systems, extensive subcortical neural processing takes place in the auditory system, and various perceptual abilities can apparently be accounted for by the subcortical encoding of particular sound features. Consequently, the role of the auditory cortex is still poorly understood. In order to address this question, we have used a combination of neurometric and psychometric approaches to investigate how the firing of neurons in auditory cortex relates to the way in which sounds are heard. In addition, we have examined the behavioural consequences of manipulating neural activity in the cortex using both pharmacological approaches and a chromophore-targeted neuronal degeneration technique. This talk will consider how spatial and non-spatial aspects of sound are represented in the auditory cortex and then focus on its role in sound localization. In particular, our studies of training-induced plasticity highlight the importance of interactions between cortical and subcortical processing in forming new associations between the physical cues that underlie sound localization and directions in space.

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SA10

Imaging the cortical and subcortical representation of pain and its modulation

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Until recently it has been difficult to obtain reliable objective information from normal subjects and patients regarding their subjective pain experience. Relating specific neurophysiologic markers to perceptual changes induced by peripheral or central sensitisation, behavioural, psychological or pharmacological mechanisms and identifying their site of action within the CNS has been a major goal for scientists, clinicians and the pharmaceutical industry. This information provides a powerful means of understanding not only the central mechanisms contributing to the chronicity of pain states but more importantly potential diagnostic information (1). Identifying non-invasively where plasticity, sensitisation and other amplification processes might occur along the pain neuraxis for an individual and relating this to their specific pain experience or measure of pain relief has considerable value. It allows a better understanding of what drives and maintains their pain state thereby allowing more appropriate selection and targeting of treatment options. With the advent of functional neuroimaging methods, such as functional magnetic resonance imaging (FMRI), positron emission tomography (PET), electroencephalography (EEG) and magnetoencephalography (MEG) this has been made feasible. Robust and reproducible activation in response to nociceptive stimulation within the human brain and spinal cord has been shown. This activation, often considered an "objective" readout of the subjective phenomenon, can be related to what the subject describes, allowing issues such as how anxiety, depression, attention, etc. alter a pain perception to be better understood at a neuroanatomical level. This provides not only potential diagnostic information but also targets for intervention. Over the past ten years, we have performed several experiments that have specifically isolated areas of cortex and brainstem that are central to the processes of expecting pain, being anxious or depressed about pain and altering your attention to pain (2-4). Furthermore, the central relevance of descending brainstem modulatory pathways in the generation and maintenance of chronic pain states in clinical conditions is becoming increasingly accepted. Advances in our ability to image this challenging area have been developed in our laboratory (5, 6) and many examples of dysfunction in this system are now found across various chronic pain conditions (7). More recently, pharmacological functional magnetic resonance imaging (phMRI) has been developed and applied to the field of pain research within our laboratory (8). Again, many advances have been made that illustrate the neural correlates of analgesia in the human brain (9). New thoughts related to how pain and pleasure interact force us to broaden our understanding of relief mechanisms and well-being (10). Finally, recent advances in our ability to image functional activation in the human spinal cord show considerable promise and provide a novel and exciting area of further investigation (11). In summary, functional imaging methods provide a powerful means to directly examine pain mechanisms in human subjects and patients at a systems level, providing potential diagnostic information as well as identifying targets for therapeutic intervention.

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SA11

Cortical processing of olfactory and taste stimuli

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The orbitofrontal cortex contains the secondary taste and olfactory cortices, in which the reward value of the taste, smell, sight and texture of food in the mouth is represented, as shown by neuronal recordings (Rolls 2005). The insular (primary) taste cortex combines taste, oral texture, and oral temperature inputs, but not olfactory or visual inputs. The visual and olfactory multimodal representations in the orbitofrontal cortex are built by visual-to-taste and olfactory-to-taste association learning. The ability of different neurons to respond to different combinations of these inputs underlies the basis of flavour. The orbitofrontal cortex neurons only respond to the taste, smell and/or sight of food if hunger is present, that is they represent the reward value of food. Moreover, sensory-specific satiety is implemented in the orbitofrontal cortex.

With human fMRI that builds on these foundations, it has been shown that the reward value of food, and its subjective correlate, the pleasantness of the flavor of food, is represented in the orbitofrontal cortex. Olfactory and taste inputs can combine non-linearly in the orbitofrontal cortex and anterior cingulate cortex to produce a representation of umami flavour from glutamate taste and a savoury odour. This leads to the concept that umami can be thought of as a delicious flavour, made delicious by a combination of a glutamate taste and a corresponding savoury odour, which are brought together only in and after the secondary taste and olfactory cortices in the brain.

The human taste, olfactory, and food flavor system in the orbitofrontal cortex and pregenual cingulate cortex can be modulated by cognitive word-level descriptors of a food being delivered, showing that cognitive effects important in the control of food intake can modulate neural processing at the first stage of the cortical processing at which the reward value and pleasantness is made explicit in the representation. Moreover, paying attention to the pleasantness of a taste or flavor enhances processing in brain regions such as the orbitofrontal cortex, whereas paying attention to intensity enhances processing in brain regions such as the insular taste cortex. It has also been shown that individual differences in the liking of foods can be predicted from the brain responses to the food, as an fMRI study in chocolate cravers vs non-cravers showed.

The orbitofrontal cortex projects to other brain regions such as the hypothalamus which are important in the control of food intake, providing the sensory signals that are modulated by hunger vs satiety signals. This approach has implications for understanding the mechanisms of obesity. The orbitofrontal cortex also projects to medial prefrontal cortex area 10, important in probabilistic decision-making.

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SA12

Feedforward and feedback processing for the grouping of image elements in visual perception

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A fundamental task of vision is to group the image elements that belong to one object and to segregate them from other objects and the background. I will discuss a conceptual framework that explains how perceptual grouping is implemented in the visual cortex. According to this framework, two mechanisms are responsible for perceptual grouping: base-grouping and incremental grouping. Base-groupings are coded by single neurons tuned to multiple features, like the combination of a color and an orientation. They are computed rapidly because they reflect the selectivity of feedforward connections that propagate information from lower to higher areas of the visual cortex. However, not all conceivable feature combinations are coded by dedicated neurons. Therefore, a second, flexible form of grouping is required that is called incremental grouping.

Incremental grouping takes more time than base-grouping because it relies also on horizontal connections between neurons in the same area and feedback connections that propagate information from higher to lower areas. These connections spread an enhanced response to all the neurons that code image elements that belong to the same perceptual object. This response enhancement acts as a label that tags those neurons that respond to image elements to be bound in perception. The enhancement of neuronal activity during incremental grouping has a correlate in psychology because attention is directed to precisely those features that are labeled by the enhanced neuronal response.

Recent evidence indicates that feedforward and feedback processing rely in part on different receptors for glutamate, the major excitatory neurotransmitter of the nervous system. Feedforward processing mainly relies on AMPA receptors that drive the neurons whereas feedback processing involves a larger contribution of NMDA receptors that are modulatory. Feedforward and feedback connections are responsible for the interactions between lower and higher areas of the visual cortex, and insight into these interactions is essential to understand the processes of base- and incremental grouping.

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SA13

Descending control of spinal nociception: its role in sensorimotor integration

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Descending control of spinal nociception is a major determinant of acute and chronic pain. The periaqueductal grey (PAG) is a major source of descending control and plays a critical role in co-ordinating functions essential for survival. These include cardiovascular regulation, sensory modulation and a variety of emotionally-related behaviours, including highly characteristic defensive responses triggered by aversive (fearful) or painful events. To date, attention has focused on mechanisms underlying autonomic and sensory aspects of PAG function, and polysynaptic descending pathways that modulate autonomic outflow and sensory processing at the level of the spinal cord are well described. In contrast, much less is known about the neural pathways and mechanisms that link PAG activity to distinct patterns of motor response; and whether descending control of sensory signals by the PAG extends to those signals that feed into (and can modify) supraspinal motor circuits that co-ordinate movement.

This is a significant gap in our knowledge given the survival value of initiating, adapting or maintaining co-ordinated motor responses in aversive or threatening situations ('active coping'; generated by output from the dorsolateral/lateral (dl/l) PAG), or of depressing motor activity during recuperation or chronic pain ('passive coping'; generated by output from the ventrolateral (vl) PAG).

The presentation will review current understanding of descending control of spinal nociception from the PAG in the context of its behavioural and clinical significance. It will then focus on recent studies that have investigated the descending control of sensory, in particular nociceptive, inputs to the cerebellum (the largest sensorimotor structure in the brain) and how this relates to movement control.

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

SA14

Hippocampal encoding of a touch-guided behavior

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Understanding the mechanisms by which sensory experiences are stored is a longstanding challenge for neuroscience. Previous work has described how the activity of neurons in the sensory cortex allows rats to discriminate the physical features of an object contacted with their whiskers. But to date there is no evidence about how neurons represent the behavioral significance of tactile stimuli, or how tactile events are encoded in memory. I will review our knowledge of sensory coding in the neocortex and then describe new data fom the hippocampus. We recorded single-unit firing and local field potentials from the CA1 region of hippocampus while rats performed a tactile task. On each trial, the rat touched a plate with its whiskers and, after identifying the texture of the plate, turned to the left or right to obtain its reward. Two textures were associated with each reward location. Over one-third of the sampled neurons encoded the identity of the texture: their firing differed for the two stimuli associated with the same reward location. Over 80% of the sampled neurons encoded the behavioral significance of the contacted texture: their firing differed according to texture category, namely the reward location with which it was associated. Texture and reward location signals were present continuously, from the moment of stimulus contact through the entire period of reward collection. The local field potential power spectrum varied across the different phases of behavior, showing that signals of single-units were integrated within a sequence of different hippocampal states.

The influence of context was examined by training rats to perform the same task in different positions within the room. The response of neurons to a given stimulus in the second context was independent of their response to that same stimulus in the first context.

These results demonstrate that hippocampal neurons encode both spatial (reward location) and nonspatial variables (stimulus identity). Furthermore, in a given neuron the presence or strength of a spatial signal did not predict the presence or strength of a nonspatial signal. Thus, there is no apparent segregation of spatial and nonspatial information. The recruitment of the population of neurons into the representation of any two events is independent.

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SA15

Vomeronasal influences on behaviour

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Recent molecular biological advances have led to a revolution in our understanding of the vomeronasal system's role in the control of rodent behaviour. This chemosensory system, which is found in most vertebrates, functions in parallel with the main olfactory system and is specialised for the detection of involatile sources of chemosignals, such as skin secretions and territorial

marks. Analysis of the mouse genome has revealed a surprisingly rich diversity of vomeronasal receptors with a total of around 260 receptor types, belonging to 3 unrelated gene families[1]. As yet the ligands for most of these receptors remain to be identified, but the range of known vomeronasal stimuli continues to expand and includes small volatile molecules, peptides and proteins[2]. These chemosignals convey key social information such as the sex and individual identity of the producer, as well as their endocrine and disease status. Certain behaviours, such as aggressive interactions among male mice, appear to be dependent on vomeronasal sensory input, as they are not observed in animals in which vomeronasal function has been disrupted. Our understanding of how male mouse sexual behaviour is switched to aggressive behaviour in the presence of a potential competitor is far from complete. However, an anatomical basis for this switch may reside in the inhibitory interactions in the neural pathways conveying vomeronasal information about male and female chemosignals, via their projections to hypothalamic areas[3].

Pheromonal effects on mammalian behaviour are quite variable and are heavily influenced by context and prior experience. Part of this variability arises from the integrated roles of the main olfactory and vomeronasal systems. There are considerable overlaps, both in stimuli that can be sensed by each system and in their projections to the medial amygdala[4], which plays a major role in social recognition. Certain involatile components of male mouse urine, most probably major urinary proteins, appear to be innately rewarding, and can support associative learning of volatile odours sensed by the main olfactory system[5]. This integration of information is likely to occur at the level of the medial amygdala and results in conditioned main olfactory cues reinforcing the behavioural response to vomeronasal stimuli.

Learning can also influence responses by gating the transmission of vomeronasal information. Female mice learn to recognise the individual chemosensory signature of their mate during a sensitive period after mating. Formation of this memory is dependent on noradrenergic transmission and appears to be associated with a long-lasting increase in the inhibitory control of mitral/tufted cell projection neurons in the accessory olfactory bulb. This increased gain of granule cell feedback inhibition is proposed to underlie recognition by selectively blocking the transmission of the mate's chemosensory signal, at the first stage of sensory processing[6]. Thus the mating male's chemosignals are less effective in activating downstream neurons in the medial amygdala and arcuate hypothalamus than chemosignals of a male to which the female has been exposed without mating. Interestingly, memory formation is associated with a dramatic and long-lasting increase in the power of local field potential oscillations in the accessory olfactory bulb[7]. This suggests that learning involves major changes in the oscillatory dynamics of the neural system and that "life events" such as mating can have long-term influences on the physiological and behavioural responses to vomeronasal stimuli.

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SA16

Emergence of action based sensory encoding in spinal sensorimotor modules - role of fetal movements

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The concept of a modular organisation of the spinal withdrawal reflex circuits has proven to be fundamental for the understanding of how the spinal cord is organised and how the sensorimotor circuits translate sensory information into adequate movement corrections. Through cross modality learning dependent mechanisms a task related body representation is engraved at the network level involving an active probing procedure termed 'somatosensory imprinting' during development. Somatosensory imprinting depends on the tactile input that is associated with spontaneous movements that occur during sleep and results in elimination of erroneous connections and establishment of correct connections. Spontaneous movements are primarily generated in the central nervous system as they still occur after complete dorsal rhizotomy. Recently we found that a task related body representation closely related to motor patterns emerges from a transitory floating and plastic organization through profound activity dependent rewiring, involving both sprouting and elimination of afferent connections. In this NMDA dependent process, tactile fibres appear to guide nociceptive afferents to appropriate targets in the spinal cord, resulting in a topographical alignment of different sensory modalities in the dorsal horn. Given that spontaneous movements are a ubiquitous phenomenon during embryonic development in all vertebrates, somatosensory imprinting may be a general strategy employed by the nervous system during developmental self-organisation.

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SA17

What a single neuron contributes to perception and behaviour

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The relationship between the activity of individual neurons and behavior is a core interest of neurobiology. Extracellular recording and stimulation techniques and have demonstrated that single neuron activity of neurons is closely correlated with behavior in mammals, but both techniques are not suited to

pinpoint the impact of single neuron activity on behavior. We confront this problem by stimulating single neurons in the rat vibrissal system and testing the effect on vibrissal movement and sensation. This approach reverses conventional physiological research, where APs are mainly studied as correlates of sensorimotor processing. Specifically we addressed this issue by assessing effects of single cell stimulation in (i) the vibrissal motor cortex (ii) the vibrissal motor neurons in the facial nucleus, (iii) in the somatosensory cortex of awake rats. In vibrissa motor cortex we find that AP initiation in individual cells causes long sequences of small and slow multi whisker movements. AP number had only little effect on whisker movement amplitude but it strongly affected movement latency. AP frequency in contrast did not affect movement latency but determined movement amplitude and direction. In the facial nucleus we find that AP initiation in individual cells causes mainly but not exclusively single whisker movements. Movements are brief and usually fast and each spike causes a very similar fixed latency movement. Thus, motor cortical neurons and cells in the facial nucleus code movements in very different ways: Cortical APs affect movements on long time scales and APs are read as sequences or "words", such that the effect (movement latency and direction) of an AP depends on the AP context. In contrast, facial nucleus APs are translated spike by spike to movement twitches. We also investigated sensory effects of single cell stimulation in the somatosensory cortex. To this end animals were first trained to report trains of cortical microstimulation pulses by a tongue lick. Once the animal reported small microstimulation currents, microstimulation trials were mixed with trials in which we evoked ~ 14 APs in single cortical neurons. Rats responded significantly more often after single cell stimulation than in catch trials without stimulation. The bias introduced by single cell stimulation was weak on average but could be strong for individual cells. We conclude that the activity of single sensory cortical neurons can lead to a behaviorally reportable effect. Thus, single neuron stimulation in general and the parametric variation of initiated AP patterns in particular, allow us to decode (i.e. measure effects of APs and AP train parameters) single neuron activity in an unprecedented fashion.

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SA18

Feedforward and feedback learning in human sensorimotor control

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When we learn a new skill, sensory feedback from previous errors are incorporated into the feedforward motor command to gradually refine our movements. I will describe a new model of motor learning based on the brain simultaneously optimizing stability, accuracy and efficiency. This model of motor learning offers new insights as to how the brain controls the complex musculoskeletal system and iteratively adjusts motor commands to improve motor skills with practice. However learning can also be used to adjust the feedback control. I will discuss two experiments in which we examined adaptation of a visuomotor reflex both to the statistics of perturbations and during learning to perturbations to dynamics of the limb. We show modulation of reflex magnitude in the absence of a fixed change in the environment, and show that reflexes are sensitive to the statistics of tasks with modulation depending on whether the variability is task relevant or task irrelevant. In addition we show transitory changes in visuomotor reflexes during dynamic learning.

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