Sensory Transduction and Subjective Experience

Expression of eight genes in three senses suggests a radical model of consciousness

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21st June 2007

Abstract: *Recent research into whole genome mapping of the mouse brain has made possible direct investigation of the brain expression of unusual genes. A search of the Allen Brain Atlas database has provided genetic and neuro-anatomical evidence for widespread specific expression in the brain of eight genes specific to sensory transduction, in vision, hearing and touch. A novel biophysical model is proposed for the function of these proteins, in generating the internal model of experiential reality.*

Introduction

Recent research in whole genome mapping of the mouse brain [1,2] has made it possible to investigate the potential central nervous function of genes that might otherwise be associated primarily with peripheral sensory transduction. At the same time, the actual molecules involved in sense transduction, in vision, hearing and touch are being characterized. The first putative transduction molecule for mammalian touch, stomatin-like protein 3 (SLP3, or Stoml3) was reported this year in Nature [3], and putative molecules in the auditory transduction pathway, epsin [4,5], and cadherin 23 (otocadherin) [5] have only been reported in the last five years and otoferlin [6,7] in 2006. Research into the genetic evolution of the visual system has also unearthed provocative new findings about vision, which became the trigger for this hypothesis. In parallel with the usual cilia-based photo-transducer molecule c-opsin are retinal ganglion cells, which use melanopsin, or r-opsin related to insect opsins (based on organelles called rhabdomeres), which depolarize rather than hyperpolarize [8]. It has also been discovered that both types of opsin work in opposition in the reptile parietal (pineal) eye [9].

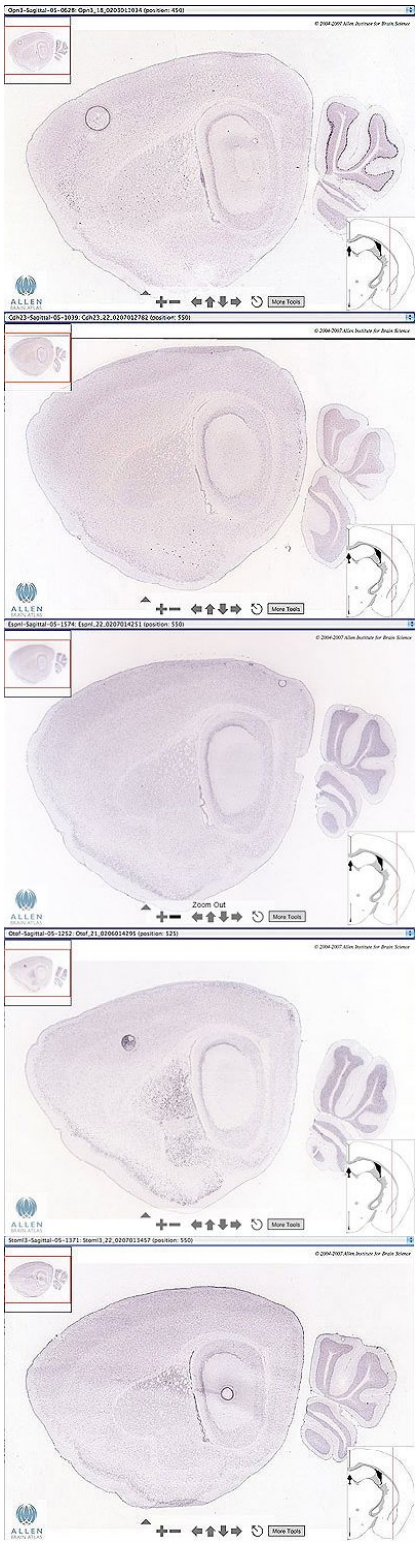

Figure 1: Large scale mouse brain expression profiles of encephalopsin (Opn3), otocadherin (Cdh23), espin (Espnl), otoferlin (Otof) and Stom3 (Allen Brain Atlas[1]) illustrate the wide and discretely specific expression of sensory transduction molecules for three senses, vision, hearing and touch in the central nervous system. Does this mean that the 'internal model of reality' evokes subjective experience using similar molecules to the physical senses?

Investigation

Interest in such idiosyncratic incidences of sensory genes became the stimulus for making a short investigation of molecules associated with sensory transduction in brain tissues, using the Allen Brain Atlas [1] of the mouse. This immediately threw up a further opsin variant, encephalopsin [10], discovered in 1999 and known to have a broad and selective distribution in the brain, including, but not restricted to, areas involved in visual processing. At the same time as making this search, Nature reported the discovery of Stoml3 in touch transduction [3] and a search revealed this also has a wide brain distribution. Stoml3 was found to bind specifically to acid-sensitive ion channels ASIC2 and 3 and a search likewise found a CNS-wide expression of these genes. Finally a search was made for auditory molecules, which threw up epsin and cadherin-23 [4,5], which likewise show brain-wide specific expression. Subsequently, the recent characterization of otoferlin [6,7], claimed to be key to the sensitivity of auditory transduction led to exploration of this auditory molecule as well, providing evidence of wide-spread expression from five genes involving three senses.

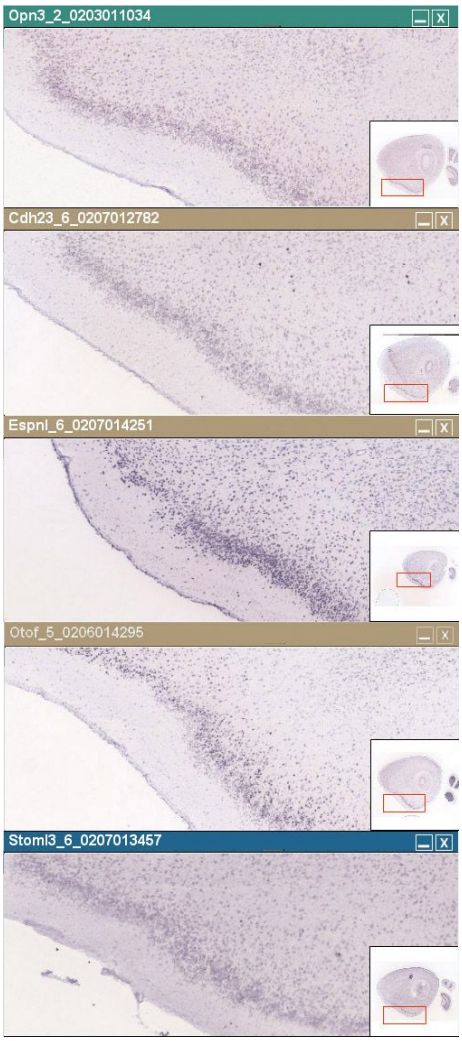

Figure 2: Exploded view in the lateral ventral cortex at the cellular level of expression of encephalopsin (Opn3), otocadherin (Cdh23), espin (Espnl), otoferlin (Otof) and Stom3 demonstrate specific expression of a similar type in cortical tissue at the cellular level.

In support of the central nervous expression of genes believed to be associated primarily with sensory transduction, an exploration of: *(a) rhodopsin, and encephalopsin, (b) otocadherin, espin, and otoferlin and (c) acid-sensitive ion channels ASIC2 and 3 and stomatin-like protein 3* using the Allen Brain Atlas is included in the figures. Figure 1 shows lateral sagittal views of the whole mouse brain for five of these genes, supporting their expression in the brain. Figure 2 Figure 2 looks in detail at an area of the ventral lateral cortex illustrating similar expression of each of these genes at the cellular level. Figure 3 shows the specific expression of rhodopsin in the cortex focused in areas consistent with visual function. Figure 4 exemplifies more specialized activity of two of them in the olfactory bulbs and cerebellum. Figure 5 shows varying expression for four of the genes in the parietal cortex.

Could the CNS contain Transduction Cascades?

Opsins are clearly transducers from photonic to electrochemical. Encephalopsin is also expressed in other organs, and is also referred to as panopsin, so could have another generalized cellular function. However there are several other opsins of interest expressed in the CNS. Pinopsin is not confined to the pineal but also occurs widely in the brain. In addition vertebrate ancient opsin is also expressed in regions bordering the pineal. Rhodopsin has activity concentrated in individual neurons across the cortex with a specific focus in the occipital, consistent with a function in the primary visual cortex.

Otoferlin, which was only characterized in Oct 2006, is as close as research can establish to the transduction step. Otoferlin functions right in the critical steps of the signaling cascade stimulating the fast kinetics of the most mature Ca dependent neurotransmitter vesicles, thus triggering the receptor cell response, and it's also transmembrane and possibly a Ca channel so it is right on the transduction interface. In particular Parsons [6] notes that the hair cell has evolved a unique calcium-sensing molecule, otoferlin, for controlling neurotransmitter release. The action of otoferlin allows a hair cell's specialized synapses — ribbon synapses, a specific class of afferent synapse common to sensory systems — to meet the requirements of hearing. Roux et. al. [7] describes otoferlin as a novel protein and transmembrane cochlear-expressed gene. So its function looks like a Ca^{++} ion channel or channel modulator that excites mature kinetically unstable vesicles. This could be the direct result of a phononic or solitonic event in the membrane.

The presence of no less than three molecules from the auditory transduction pathway - otoferlin, otocadherin and espin in the CNS suggests functional linkage in the CNS and a possible signaling cascade. All three don't have to be directly involved in transduction, but all may be essential to it, as is evidenced by deafness studies.

SLP3 is a transduction modulator, which binds specifically to acid-sensitive ion channels ASIC 2&3. The atlas found very similar cortical distributions of all three molecules, again setting up a putative model for a transduction cascade here as well. However ASIC may have more general ion-channel functions in the CNS which makes the role of SLP3 interesting. Wetzal et. al. [3] show mechano-sensitive ion channels found in many sensory neurons do not function without SLP3 including touch mechanoreceptors as a whole and cites their coupling to ASIC 2&3.

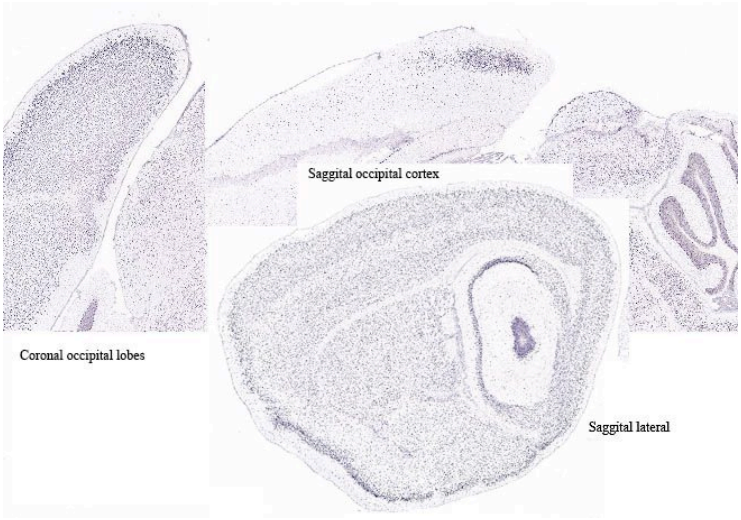

Figure 3: Expression of rhodopsin in the CNS shows both strong selective neuronal expression and a focal expression in the occipital cortex consistent with expression in the primary visual areas.

Subjective Consciousness and Biophysical Transduction

Interest in the biophysical basis of subjective consciousness has become central to the emerging area of consciousness research. A variety of models have been put forward for the involvement of CNS proteins in, quantum computation by orchestrated objective reduction in microtubules[12,13,14], and others involving coherent quantum excitations including a protein/water/EM field model[15,16,17,18]. A variety of functional proteins in the CNS are under investigation to test for their possible role in the biophysical underpinning of subjective consciousness. It has also been proposed that conscious anticipation might be made possible through quantum excitations both emitted and absorbed by the CNS [27,28].

Although subjective consciousness has many attributes, from the sense of self-awareness (self-consciousness) through semantic and rational processes (rational mind) and working memory, some of which involve subliminal processing on the fringes of consciousness or unconsciously, there is a major central arena of conscious experience, sometimes referred to as the Cartesian theatre [19,20], which gives the subjective expression of an envelope of sensory experience, whether it involves experiences of the external world or purely internal states such as dreaming. This in turn gives rise to the notorious binding problem – how a distributed parallel processing organ like the cortex with disparate sensory areas can bring in all back together. However the primacy of internal 'sensory experience' in subjective consciousness suggests a biophysical support based on the same principles as are involved in sensory transduction.

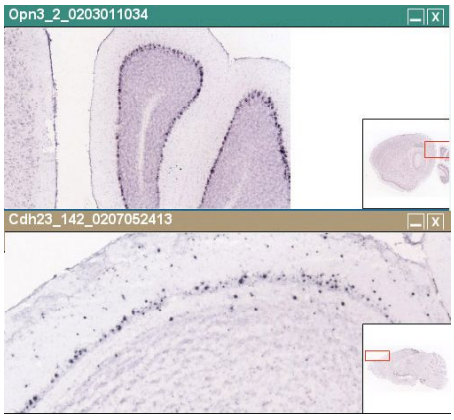

Figure 4: Specialized expression of encephalopsin (Opn3) in the cerebellum, and of otocadherin (Cdh23) in the olfactory lobes illustrate divergent specialized function of these genes in specific brain areas contrasting with their similar expression in figure 2.

The occurrence of putative sensory transduction genes in the central nervous system is consistent with a novel biophysical model supporting subjective consciousness – that the distributed functioning of the central nervous system provides an 'internal sensory system' which can generate abstracted sensory experiences of reality forming an 'internal model of reality' using the same physical principles as are involved in sensory transduction in a bi-directional manner, enabling coherent generation and reception of biophysical excitations, particularly those associated with vision and audition. Olfaction has a fundamentally different basis, both in brain architecture and in the fact that it involves specific molecular receptors, which cannot regenerate their stimuli by reverse transduction, although there is evidence for olfactory synesthesia [21,22]. Some forms of synesthesia, such as responding with feeling to seeing another person's finger touched [23], may also involve specific interactive circuitry, including mirror neurons [24].

The model gives a succinct explanation of why subjective experience such, as dream, memory and reflection, as Carl Jung [25] put it, so successfully evokes the deep qualitative differences between the senses, when a purely electrochemical model has no qualitative differences between the senses, except in terms of differential developmental and stimulus-induced processing connectivities. The wide distribution of each of these molecules, not confined to one sensory area, suggests that the evolution of the cortex as an adaptable system, has resulted in a flexible design, in which widespread areas of

the brain may be capable of generating dynamics simulating more than one sensory process biophysically, consistent with descriptions of kaleidoscopic synesthesia [21] in the medical literature, in psychedelic folklore, and manifest in ancient cave art running far back into our human origins [26].

By contrast with all other areas of scientific discovery, from the human genome to cosmological grand unification, the nature and basis of conscious experience remains the principal scientific area in the third millennium for which there is yet no realizable candidate theory, nor even a qualitative understanding in principle, of how our 'internal model of reality' is generated. While consciousness research has come in from the cold as an accepted scientific research area [12,27], there are still major stumbling blocks to a realizable theory of consciousness, including the 'hard problem' [30] – whether subjective consciousness is in any way qualitatively identifiable with an objective description of reality, to the 'binding problem' - how multifarious processes come together to convey the impression of a 'Cartesian theatre' [19,20] of the mind.

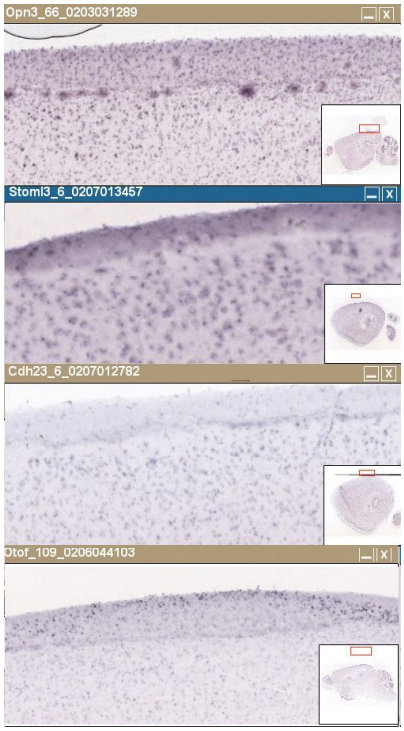

Figure 5: Expression of encephalopsin (Opn3), stoml3, otocadherin (Cdh23) and otoferlin (Otof) in the parietal cortex illustrate differing modes of cortical expression.

Research into the biophysical basis of consciousness remains obscure, invoking a variety of speculative theories, few of which have convincing experimental support at the cellular level. Nevertheless subjective conscious states, from dreaming, through psychedelic states, to memory and imagination, each possess a veridical reality, which is of the same broad sensory nature as an external experience. Indeed dreaming can become all too real, by any sensory measure, despite attempts at lucidity checks!

Although we conceive of the nominal five senses - vision, touch, hearing taste and smell - as biological adaptions, they are actually manifestations of the principal quantum modes by which an organism can interact with the physical world. Vision is photon-orbital interaction, hearing comes somewhere between phonon-orbital and the mechano-receptor dynamics of touch, taste and smell are traditionally defined as an orbital-orbital shape-fitting, although some research [29] suggests smell involves quantum vibration modes as well. Sensory transduction is also capable of working at the quantum limit. Frog rod cells are capable of responding to single photons [26], pheromones likewise can elicit a response from a single molecule (especially in insects) and the limits of audition involve movements of the cochlear membrane of the order of a hydrogen atom radius [26,27].

While the evidence presented is from distributed gene expression and thus in no way confirms these molecules are performing a sensory transduction function in the central nervous system, the theory does present an innovative and scientifically provocative biophysical hypothesis about the genesis of the 'internal model', which could also have significant implications for cognitive science. Physically transduced quantum excitations phase correlated with the electrodynamics underlying the electroencephalogram could provide a realizable means for the brain to generate quantum entangled states, permitting forms of quantum computing using our massively parallel, phase coupled brain dynamics. Some models [27,28] also suggest such processes could also have an anticipatory function which might help explain free-will.

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