HYPOTHESIS

A hypothesis to explain how the sensory cortices respond in the appropriate sensory mode

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SUMMARY

How does an area of sensory cortex recognize the specific nature of the sensory mode of the stimulus that arrives from the peripheral sensory receptor, when nerve impulses are only all-or-nothing action potentials? Work in animals has shown that an area of sensory cortex can learn in which mode to respond. A period of cortical learning is required for phantom limb phenomena to develop, and for the ocular blind to dream in the visual mode. Arguing from these facts I develop the hypothesis that within the sensory cortices there are neurons that learn by neurotropic factor transport from their sensory receptors to function as surrogates for those receptors, thus enabling sensory cortical response to be modally specific.

INTRODUCTION

How does an area of sensory cortex recognize the specific nature of the sensory mode of the stimulus that arrives from the peripheral sensory receptor? Nerve impulses are electrical signals which convey information as action potentials without voltage variation. There is no modulation of the signal other than by variation in the number and distribution of the pulses. Differences in quality of a sensation are transmitted via a multichannel arrangement using a vast number of nerve fibres each encoding a different sensory quality—the doctrine of specific nerve energies[1]. Does this enable the sensory cortex to respond appropriately to the modal quality of the stimulus? Humphrey[2], for example, does not think so. Kolb and Whishaw[3] put forward three other possible explanations. One is that each sensory system has a preferred link with certain kinds of movement to ensure that each sensory system remains distinct at every level of neural organization. Certainly Young[1] points out that action completes decoding, thus enabling recognition. But this theory seems to present a circular argument which does not address modal recognition. Their second explanation is that the sensory cortical areas that process different sensations are inherently different. Rewiring experiments in animals negate this theory. In neonatal ferrets retinal inputs were redirected to the auditory thalamus and the animals were raised to adulthood. These animals then responded to light as though they were receiving visual rather than auditory stimuli; they behaved as though they could see on the rewired side of the brain[4]. This tells us that a specific sensory mode was not inherent in that sensory cortex: an area that normally has an auditory function was able to respond in a visual manner. Kolb and Whishaw's third explanation is that we learn to distinguish the different sensory modalities through experience—a pattern-of-inputs theory. Consider the visual mode. There is a large amount of experimentally based evidence about the details of visual cortical function, about how the information from the retina is dissected, and about the role given to each segment of that information. But how does the visual cortex reproduce the retinal image in the visual mode? According to the pattern-of-input theory this results from the functional connectivity between photoreceptors and visual cortical neurons: coactivation of the firing activity of the large number of nerve fibres that eventually impinge on these neurons results in patterns of dendritic input that create the modality-specific visual response of those neurons.

Given that such connectivity could determine how occipital cortical neurons respond in the visual mode, the question is how they do so once that functional connectivity has been lost, as happens in dreams of the ocular blind. From two well established sets of observations, I argue that, within the different sensory cortices, certain neurons have differentiated phenotypically so as to respond in the appropriate sensory modality—that such differentiation is brought about by the action of neurotropic factors originating from the stimulated sensory receptor and transported along neurites and across intermediary neurons, ultimately to reach the cortical sensory neurons where they promote new gene expression. The resultant phenotype enables neuronal response to be modally specific.

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OBSERVATIONS

Phantom limbs

Let us consider the somatosensory modes. Provided there is neural connectivity between the site of the integumentary stimulus and the relevant sensory cortex, then one appreciates the nature of the stimulus. That stimulus is detected by sensory receptors responsive to touch, heat, cold, or pressure, and the somatosensory cortex of the brain is able to register correctly the nature of that stimulus. We know that nerve impulses are electrical signals which convey information as action potentials without voltage variation. The cortex receives sensory information from large numbers of nerve fibres each conveying a different quality of the stimulus. But each fibre conveys this information as does each other fibre by all-or-nothing action potentials. So how does a somatosensory cortical neuron recognize from the impulses it is receiving that the peripheral stimulus is one of touch, heat, cold, or pressure?

Consider the phenomenology of phantom limbs[5]. After limb amputation nearly all adults experience a phantom limb. Amputees may feel that the phantom adopts a habitual posture or that its posture changes spontaneously. Some describe the continued feeling of a wedding ring or of a watch band. That is to say, the sensory cortex representing the amputated limb continues to function without sensory stimuli from the now absent limb. After the amputation, neural plasticity results in reorganized cortical connections with cortical rerouting/re-mapping[5]. Since the cortical representations of the hand and face are juxtaposed in the sensory homunculus, on-routing results in the spread of the facial area into the hand area. Afferent impulses from the face now communicate additionally with cortical sensory neurons representing the hand. This provides access to the cortex representing the amputated limb. Thus a touch on the amputee's face is felt as touch on the phantom hand as well as on the face. Modal specificity is preserved; a warm or a cold stimulus to the face is felt as warmth or cold on the phantom. The somatosensory cortex representing the amputated limb continues to respond in the appropriate sensory mode after severance from the peripheral sensory receptor.

Phantom limbs are experienced far less often in early childhood, though near universal by the age of eight. Seemingly, for a post-amputation phantom limb to develop, a certain period of neural input from limb to brain is required before the somatosensory neurons can be independent of the peripheral sensory receptors. That is, a learning period is needed for those neurons to permanently acquire that verisimilar sensory receptor function (touch, temperature, sense of position) which they are then able to retain after severance from those peripheral sensory receptors. This takes some years.

Dreams of the blind

Now let us return to the visual mode. As a result of anatomical connectivity with the retina, cortical visual processing begins in the primary or striate visual cortex of the occipital lobes and continues into the extra-striate areas as shown by microelectrode recording studies. Imaging techniques suggest that these visual cortical areas are the site of visual perception. Electrophysiological and imaging investigations recorded during the exercise of visual imagination reveal enhanced activity in these same visual cortical regions. A person who has sustained damage to his or her visual cortex has a defect in external visual perception. That defect corresponds to the area of visual cortical damage. During visual imagination the person's internal visual imagery displays the same localized defect. Thus visual perception whether externally generated (from the eyes) or internally generated (from the imagination) utilizes the same neural substrate of the visual cortex[6]. Similarly in dream images deficits occur which correlate with areas of visual cortical brain damage, indicating that the same neural substrate of the visual cortex is used for the visual content of the dream image[7].

Just as the somatosensory cortex must respond in the appropriate sensory mode, so must the visual cortex during both perception and dreaming. What evidence is there that in the visual cortex there are neurons that respond to a neural stimulus from the retina in a verisimilar manner to that of photoreceptors? This evidence comes from dreams of the blind[8]. Persons who are congenitally blind or who become blind in early childhood do not have visual dreams. However, if blindness due to ocular disease supervenes after early childhood that person continues to experience visual dreams. This tells us that, in those people with ocular blindness, the visual cortex involved in reproducing the dream action can respond in the visual mode provided it has been given the opportunity to learn. Some five to seven years of ongoing vision are required for the visual cortex to gain this ability to respond in the visual mode. Moreover, the visual cortex retains this function even in the absence of continuing retinal connectivity because individuals who undergo bilateral eye enucleation after childhood likewise have visual dreams. This situation is similar to that of a post-amputation phantom limb in which the somatosensory cortex requires a period of time to permanently acquire the ability to respond to afferent impulses in the appropriate sensory mode.

DEVELOPMENT OF THE HYPOTHESIS

How do we explain the phenomena of phantom limbs and dreams of the blind? In particular, how do the somatosensory and visual cortices continue to function in the appropriate sensory mode after severance from their

respective sense-organs? Given that connectivity during development determines how cortical neurons respond, how do they continue to so respond after that connectivity has been severed, and then only if a substantial period of connectivity has preceded that severance? Those sensory cortical neurons have acquired the ability to continue to respond as they did before loss of sensory receptor connectivity. They now have the property of responding, modally speaking, to afferent impulses in like manner to the sensory receptors, and in this sense they are behaving as surrogate sensory receptors. In the early years of life the mechanism for sensory modal specificity resides in end-organ/sensory-neuron connectivity. However, after this time we have cortical sensory neurons that are independent of that connectivity and which continue to respond in the appropriate sensory mode, thus explaining the phenomena of phantom limbs and dreams of the blind.

There is some experimental evidence supporting the idea that there are cortical sensory neurons responsive to stimulation in a way similar to that of the appropriate sensory receptors. Thus in 1958 Penfield[9] reported that conscious patients undergoing electrical stimulation of the occipital cortex reported seeing lights, coloured stars or dark lines, and that stimulation of the superior aspect of the temporal lobes produced simple auditory responses in the nature of buzzing, humming, ringing or hissing sounds, and postcentral gyrus stimulation caused tingling or numbness or a sense of movement in the contralateral half of the body.

So far I have argued that there must be some way in which the different sensory cortical neurons recognize the nature (touch, hot, cold, light, sound) of the peripheral stimulus giving rise to the afferent nerve impulses which impinge on those neurons. These neurons must possess a property which enables them to recognize the nature of the stimulus. I have outlined two facts that provide the evidence that cortical sensory neurons acquire from the sensory receptors this ability to respond in the appropriate sensory mode. First, the sensory cortex does not possess inherent modal specificity; afferent impulses from one peripheral sense organ can instruct another area of sensory cortex to respond in that different mode. Second, a period of time is required for the development of a post-amputation phantom limb and for the realization of dreaming in the ocular blind.

What is happening during this period during which the developing infant and child is well able to see, hear and feel, smell and taste? The sensory cortical neurons, under the influence of the peripheral sensory receptors, are responding in the appropriate sensory mode and are acquiring the ability to continue to so respond after severance from those sense organs. Where else than from the sensory receptors can this learning come, given that sensory cortical modal specificity is not genetically predetermined and given that a substantial period of time is needed for this modal specific property of sensory cortical neurons to become permanently established? Learning can result from the association of nerve firing patterns and reinforcing stimuli with the coincidental depolarization of a target cortical sensory neuron; but even if this were to occur during a critical development period how is the appropriate neuronal phenotype established—appropriate to the specific sensory mode dictated by that particular sensory receptor connection? In my view it is not only nerve impulses that go from sense-organ to neuron; there is also a transfer of the property of modal specificity that enables the cortical neuron to respond in the same modality as that of the sensory receptor.

Neurotropic factors, including those supplied by target cells, promote both neuronal survival and connections in the developing nervous system; in the olfactory system odorant receptors function in axon targeting, thereby linking the sensory receptor property of one neuron to the next[10].Neuronal cell type diversity seems to be produced by neural inducing factors and transcription factors which interact with DNA to regulate gene expression and establish neuronal phenotype[10]. Sensory nerves transfer information by transport of molecules along neurites. Neurotropins include factors released from innervated target tissue, where they bind to specific receptors on the surface of the nerve terminal. This activated receptor complex is then transported to the soma of the innervating neuron, there to signal the nucleus of that neuron. This signal can promote new gene expression[11].

In a review article subtitled 'the concept of trophic currencies in neural networks' von Bartheld, Wang and Butowt[12] summarize evidence for retrograde and anterograde neurotropin transport together with transcytosis—the passage of neurotropins through neurons. This could enable target derived neurotropic factors to pass from a peripheral sensory receptor via intermediary neurons to cortical sensory neurons, including those beyond the primary sensory cortex. There these factors can promote new gene expression to establish a particular neuronal phenotype and hence a specific functional property of the neuron—namely, the ability to respond in the same modality as does the contributing peripheral sensory organ.

This concept does not demand that every synaptic input to each sensory neuron arises from the peripheral sense organ—only that sufficient so originate to deliver the neurotropins. Moreover, tropic material is not all degraded; some is recycled, some is stored. von Bartheld *et al.*[12] suggest that neurons accumulate tropic material in proportion to their successful communication with connected partners. Perhaps when a cortical sensory neuron has accumulated sufficient neurotropin its phenotype is fixed,

allowing it to function permanently in a modally relevant way.

IMPLICATIONS OF THE HYPOTHESIS

This hypothesis offers an explanation as to how the processing of afferent impulses from sensory receptor to sensory cortex becomes modality-specific and explains how such modal specificity, once acquired, allows for imagining and dreaming which are events independent of exogenous sensory input. Modal specificity refers only to the primary senses such as light (including colour), sound and touch but not to secondarily derived qualities such as movement or shape. The hypothesis requires the transport of neurotropic factors not only along dendrites and axons but across intermediary neuronal somata to and beyond the primary sensory cortices. An implication of this is that modal-specific responsiveness may be conferred on intermediary sensory neurons. Thus it has long been held that pain can be perceived at the level of the thalamus[13].

A tenet of this hypothesis is that each sensory cortex is modal-specific. How then is cross-modal processing to be explained? For example, how is the auditory cortex recruited for lip-reading in hearing subjects, in whom that cortex should respond only to sound? Processing of information could take place in the prefrontal working cortex which subsequently enlists the auditory cortex. Synaesthesia can also involve cross-modal processing. A synaesthetic experience can occur in a modality different from that of the inducing stimulus, as happens in coloured hearing. In addition to the auditory cortical response to the sound, the visual cortex has become involved, having been recruited by the neural area primarily responsible for the synaesthetic phenomenon[14].

How can the hypothesis be tested? In principle it needs to be shown that some ultrastructural or biochemical feature unique to one sensory receptor organ is found in neurons in the appropriate primary sensory cortex but not in other primary sensory cortices. For example, such a feature may be a receptor and/or transducer molecule. As more antibodies to proteins become available it should be possible to identify unique molecules present in sensory receptor organs and to test this idea empirically.

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