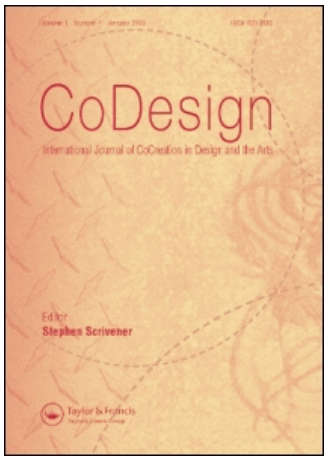

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Neuroimaging of sensory and affective experience in the human brain

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Modern neuroimaging and its potential impact on affective design is explored in this paper. Some of the recent exciting developments in neuroimaging techniques are described. The opportunities now provided by current neuroimaging tools to investigate the affective experiences of pleasure and pain are demonstrated. Neurosurgical treatment of pain is used as an example of how the causal link between brain activity and affect can be shown. These examples from our research group show how advances in neuroimaging are deepening our understanding of the affective processing that accompanies all our experiences and decisions. The paper shows how scientists and artists can work together to use neuroimaging to create unique representations of the living human brain, which may themselves help us understand the brain's function.

Keywords: Affect; Neurosurgery; Neuroscience; Pain; Pleasure

1. Introduction

Throughout history, artists and scientists have been interested in the human body but only recently have we become able to image within the living human brain. Modern brain research is one of the largest scientific challenges of this millennium, uncovering enormous complexities that can only be understood by means of multidisciplinary collaboration across traditional subject boundaries. Thus, neuroscience is not the exclusive preserve of doctors: it is dependant upon psychologists, physiologists, biologists, pharmacists, geneticists, physicists, statisticians, engineers, computer scientists and increasingly researchers from the social sciences and humanities. All can contribute to and utilise knowledge about the brain, from the level of its component molecules to its function within human society.

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The human sensory experience is a subjective phenomenon modified by multiple individual and contextual factors. For many years researchers have attempted to quantify this affective response solely by observing its effects on behaviour and the body's physiological state. Nowadays, for the first time, new neuroimaging tools allow us objectively to measure the central processing of this experience at timescales relevant to the function of the human brain. These tools provide *biomarkers* of cognitive response that can be used by researchers, designers and developers from multiple disciplines within the neuroscience team.

Today we also have the techniques and tools to modify abnormal affect which is manifest in several neurological and psychiatric disorders. By involving patients in our research we are given a unique and privileged opportunity to investigate their affective experiences and to prove the causal relationship between particular patterns of brain activity and affect. We can map changing activation of the living human brain as we modify its function over timeframes from milliseconds to decades. These neuroimaging findings can then be correlated with direct recordings from the living human brain.

Pleasure and pain are at the extremes of subjective experience. One of our most fundamental pleasures is the experience of tasting, smelling, touching, seeing and hearing what we eat. Food offers the necessary energy for survival and is along with sex perhaps the most important motivating force in life. The study of food intake allows us many insights into the fundamental function of the brain, studying not only sensory but also pleasurable affective experiences. In contrast pain is the prototypic unpleasant subjective experience. Our novel research using neuroimaging has mapped real time changes in pain. Being able to quantify the *qualia* of conscious experience in this way will give researchers and designers a powerful tool to assess the affective experience that until recently has been the territory of philosophers rather than neuroscientists.

2. Neuroimaging

Not only scientists but also a long line of artists including Leonardo da Vinci have been obsessed with understanding the inner workings of the human body. The main limitation of pre 20th century brain research was the fact that knowledge was derived from post mortem specimens. The development of methods to image the living human started with the discovery of X-rays by the German physicist Wilhelm Konrad Röntgen in 1895. This earned him a Nobel Prize in Physics in 1901. Some of the most dramatic progress in the area of neuroscience has been in the evolution of sophisticated imaging technologies that allow us to investigate the brain *in vivo*. These neuroimaging methods have only come into being through large multidisciplinary research efforts. Their continuing importance to scientific progress is reflected by the many Nobel Prizes awarded to neuroimaging techniques since Röntgen (e.g. computerised tomography in 1979 and magnetic resonance imaging in 2003, as well as several earlier Nobel Prizes awarded for research in the fundamental physical principles involved).

Neuroimaging techniques are based on three fundamental principles for studying the physical properties of biological tissue: absorption, emission and resonance (Posner and Raichle 1997, Huettel *et al*. 2004).

The brain can be irradiated and the amount of ionised radiation absorbed can be measured. This is the principle behind X-rays, as used in computerised tomography (CT). It is also possible to inject radioactive tracers in the blood and measure the amount of radiation emitted which is the method used in single photon emission computed tomography (SPECT) and positron emission tomography (PET). These techniques are

more difficult to justify in a non-medical setting as they involve small but potentially harmful doses of radiation.

Magnetic resonance imaging (MRI) is a versatile and safe technique that measures the changes in the electromagnetic resonance of biological tissue by emitting and detecting electromagnetic pulse sequences (Huettel *et al*. 2004). Extending the basic technique of MRI has enabled the mapping of the direction of passage of nerve fibres using a method called diffusion tensor imaging (DTI) and study of the biochemical composition of the brain tissue using MRI spectroscopy (MRS).

CT and MRI show the structure of the human brain, producing details equivalent to the information found in the best anatomy textbooks. Repeating these scans over months and years can give us information about how the gross structure of the brain changes with time but this information remains static. In contrast affect is a dynamic process that alters with stimulus and surroundings without gross changes in brain structure. It can only be seen using dynamic (referred to as functional) neuroimaging techniques.

Over the last decade the great advances in functional imaging have taken place using functional MRI (fMRI), and to a lesser extent PET. The signals measured with fMRI and PET can show that there have been changes in blood flow, cellular metabolism or chemical composition in certain brain regions, but they are really only showing the footprints of recent neural activity. The other limitation of these techniques is their temporal resolution—they are produced by averaging data over seconds and minutes. Unfortunately nearly all brain activity takes place extremely rapidly, over milliseconds, and neither fMRI nor PET can show more than mere shadows of this. Only this century do we have a technique that reliably keeps up with the millisecond speed of changing brain activity. Magnetoencephalography (MEG) detects the very weak electromagnetic signals that are created by current flowing along groups of nerve fibres with a temporal resolution of less than 1 ms. This is the closest we have come to non-invasively revealing the temporal structure of fundamental neural activity. Unfortunately its spatial resolution deteriorates as we study deeper inside the brain and on its own it gives little static structural detail.

By integrating multiple brain-imaging techniques we are able to comprehensively study the affective response. These techniques can show us the living brain's incredible complexity across many different time spans. Over milliseconds and seconds we can see which parts of the brain are active through changes in their electromagnetic fields and in their blood and oxygen consumption. Over minutes we can see how chemical signals, *neurotransmitters*, are released, and how they spread to nearby regions of the brain. Over even longer periods of time—month and years—we can see if the brain's structure or patterns of functional activity change when carrying out the same tasks or when experiencing the same stimuli.

3. Neuromodulation

Due to our group's neurosurgical basis we are actively involved in therapies that modify brain activity. In addition to passively recording changes in brain activity we have the ability to stimulate selected regions of the brain and measure the response, providing invaluable research data about brain processing.

The brain can be stimulated non-invasively from outside the skull using transcranial magnetic stimulation (TMS). TMS induces electrical excitation of the brain across the skull, by inducing a weak electric current in neurones using a rapidly changing magnetic field. Single pulses of TMS can be used to momentarily excite the cortex. For example a pulse of TMS over the primary motor cortex will produce a motor-evoked potential

causing a contraction of the muscle to which that area of the cortex is connected. Similarly stimulating over areas of primary sensory cortex can produce the experience of that sensation, e.g. the visual cortex will produces spots of light known as phosphenes.

Repetitive TMS (rTMS) is a technique in which the brain is repeatedly stimulated. This has the effect of increasing or decreasing the excitability of that part of the brain to normal stimuli. Whether excitation or depression is induced depends on the frequency and intensity of stimulation as well as the orientation of the stimulating coil in relation to the underlying neurones.

The American Food and Drugs Administration (FDA) is currently considering approving TMS as a treatment for major depressive disorder. It has been suggested to be helpful in a number of other medical conditions with affective components including pain but its great benefit is in research settings due to its non-surgical temporary nature.

More impressive changes in brain activity can be produced by direct stimulation of either the cortex or structures at the centre of the brain. Our translational research group led by Professor Tipu Aziz is at the forefront of this speciality known as functional neurosurgery. The effects of deep brain stimulation (DBS) are the result of careful scientific experimentation (Aziz and Stein, 2004). We and others around the world treat an increasing number of neurological conditions using these methods. Initial work in this area focused on movement disorders but more recent efforts have led to therapy for affective conditions such as depression (Mayberg *et al*. 2005) and pain (Bittar *et al*. 2005).

Animal experiments showed that chronic pain can be helped by stimulation of regions of the brain known as the periaqueductal grey and the thalamus (Reynolds 1969). This work has been translated into DBS surgery (see figure 1). It is interesting to note the anecdotal reports our patients give following this surgery. One of our most eloquent patients reported that with the stimulator switched on the pain sensation was still present but she no longer felt troubled by it. This dissociation between primary stimulus and emotional processing has also been shown with other neurosurgical procedures to treat pain that interrupt different pathways in the brain (Cohen *et al*. 2001). Our group and others are investigating how the emotional and autonomic responses to pain are represented and can be modulated (Green 2006).

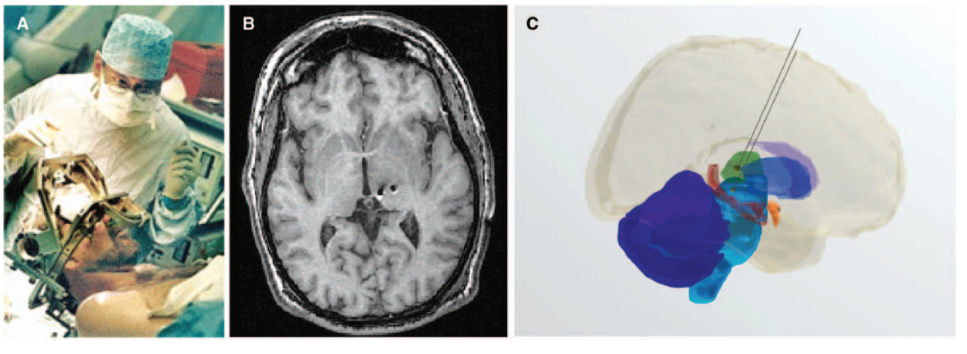

Figure 1. *Deep brain stimulation*. (A) Professor Tipu Aziz inserting a deep brain stimulator into a patient. (B) an MRI scan after surgery showing the position of the stimulator electrodes (the two small black circles near the centre of the image) in the left thalamus and perventricular grey. (C) A 3D reconstruction of the brain indicating the position of the stimulator electrodes (the two thin straight lines).

4. Neural components of affective processing

The affective experience involves many different neural processes. They can be illustrated by the sensory response to food. All of the classic five senses (vision, hearing, smell, taste, and touch) are involved in the regulation of food intake. An important computational principle of sensory processing in the brain is that the primary sensory cortices (the cortex is the highly interconnected outer surface of the brain) receive sensory information from their particular sensory nerve fibres and process this information to form neural representations of the identity of the stimulus.

No one sense in isolation produces our sensory experience. In the case of food, identifying and evaluating potential food sources begins at a distance using the olfactory and (to some extent) auditory systems which are then aided by other more precise distance and directional senses such as the visual system (Gottfried and Dolan 2003). It is important to note that there is usually a hierarchy between senses. For example, visual influences usually override the olfactory system, as demonstrated by experiments manipulating the olfactory perception of wine by artificially colouring a white wine red (Morrot *et al*. 2001).

Humans have basic protective reflexes that are activated early in the processing of any stimulus. For example, when a food is grasped and delivered to the mouth, taste, smell and somatosensory input (such as temperature, viscosity, pungency and irritation) make the vital decision of whether to swallow or reject a potentially poisonous food. These reflexes occur in deep areas of the brain, and are not altered even by the destruction of all the more complex brain regions that mammals possess (Grill and Norgren 1978).

As well as the external senses there exists a fundamental system of internal sensory receptors (the autonomic nervous system). These internal states feed back important information to the processing of external stimuli e.g. mechanical distension of the stomach contributes to satiety.

The sensory systems of taste, smell and touch are among the most fundamental building blocks of the brain's natural reward systems (Kelley and Berridge, 2002). Motivational state is crucial in determining the affective response to a fixed sensory stimulus. However, it has been shown in other, non-human, primates that the primary representation of stimulus identity remains to a large degree constant and is not modulated by motivational state (Rolls, 1999). This principle is important in forming consistent and accurate representations of the world. As we will explore, it is later in the hierarchy of brain processing that motivational state and autonomic responses are integrated to produce the combined affective response.

5. Quantifying the affective response

Affective responses involve complex brain processing. Functional neuroimaging has highlighted the areas of the brain that are affected by stimuli that, for example, excite the five basic senses of touch, sound, sight, hearing and smell (see figure 2). If one were to put a subject in an fMRI scanner and have them listen to sounds, the area of the brain that is specialised for sound and receives direct connections from the sensory organs of the ear will be active and thus show an increased blood flow (Schlosser *et al.* 1998). Similarly visual stimuli increase activity in the occipital lobe, an area of the brain that has been known to contain the seat of vision for over a hundred years (Tootell *et al*. 1996).

The ability to quantify affective responses has developed over the last decade due to advances in functional neuroimaging technologies and the development of more complex

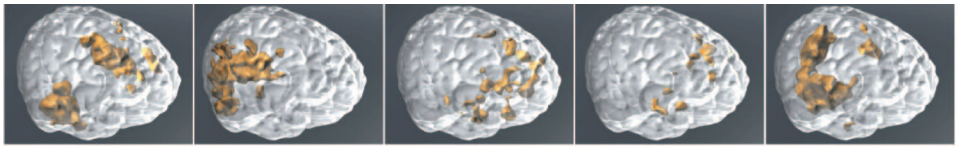

Figure 2. *fMRI of the senses*. From left to right the primary areas of the brain that are active during hearing, seeing, smelling, tasting and touching.

and powerful analytical methods. Simple mapping experiments that tended to deal with single sensory modalities are now complemented by paradigms that involve multisensory inputs. By performing these type of investigations it has been possible to delve into affective experiences such as memory (Brewer *et al*. 1998) and even gambling behaviour (O'Doherty *et al*. 2001). As part of our research we have used neuroimaging to measure cognitive activity occurring during pleasure and pain.

5.1 *Pleasure*

One way to quantify pleasure is by investigating 'selective satiety'. We have all experienced the feeling of having plenty of room and desire for the dessert despite being completely full from the main course. From an evolutionary perspective, this has the clear advantage of allowing us and other animals to obtain a sufficiently wide variety of nutrients.

Selective satiety (or 'sensory-specific satiety' as it is also known) is a particularly useful phenomenon for studying affective representation in the brain, because it provides a way of altering the affective value of a stimulus without modifying its physical attributes. As a result, any differences observed between the representation of a particular food stimulus in the brain before and after satiety can be attributed to the change in the impact of the reward, or the reward value.

We used functional magnetic resonance imaging (fMRI) to investigate the neural mechanisms related to selective satiety (Kringelbach *et al*. 2003). This fMRI process allowed us to identify the neural correlates of subjective pleasantness.

To motivate the participants properly we asked them to refrain from eating for at least 6 h prior to the experiment. They were pre-screened to ensure that they found our two stimuli (tomato juice and chocolate milk) pleasant. We also ensured that they were not overweight, dieting or even planning to go on a diet. Both chocolate milk and tomato juice were chosen to be palatable at room temperature. The clear difference in their flavour and texture helps to facilitate selective satiety effects and minimises the likelihood of the participants' developing a generalised satiety to both of the liquid foods. By controlling for all these possible confounds we are able to detect subtle differences in brain activity between the two stimuli.

For the first part of the experiment the participants were placed in the MRI scanner and scanned while being presented with each of the two liquid food stimuli, as well as a tasteless control solution which was delivered to the participant's mouth, through three tubes held between the lips. Stimuli in functional imaging protocols can take many forms. As well as taste, visual, auditory, tactile or a combination of them can be presented to the subject whilst their brain is scanned.

The trick of neuroimaging is to present the various stimuli repeatedly until statistically significant brain responses are obtained. In this experiment the liquids were delivered in

sequence and this cycle was repeated 16 times. During the imaging run, participants used a button box to indicate their subjective pleasantness of the taste stimuli on a visual rating scale ranging from +2 (very pleasant) to −2 (very unpleasant).

After the initial scanning, participants were taken out of the scanner and fed to satiety on one of the liquid foods. They were instructed to consume the liquid foods for their lunch and to drink as much of them as they could until they really did not want any more. Half the participants were fed to satiety on tomato juice and the other half were fed to satiety on the chocolate milk. In this circumstance we physically altered the context of our subsequent stimuli but in different paradigms this may be done purely cognitively by discussion or description alone.

Once the participants had finished their meal the most important part of the experiment took place: they went back into the scanner and the scanning procedure was repeated exactly as before. At this point we found that the participants reported not liking the liquid they had been fed for lunch any more, and gave it negative scores. But the same participants still liked the other stimulus which they had not been fed. It was only the difference between the two stimuli's subjective *pleasantness* ratings that had changed.

The changes in brain activity over the course of the experiment were then correlated with the subjective pleasantness ratings for all participants. Statistical analysis revealed that a part of the anterior orbitofrontal cortex was correlated with the participants' subjective experience of pleasantness.

Our studies and that of other groups have since found similar correlates of subjective experience of pleasure. Interestingly, studies of the subjective effects of amphetamine ('speed') show that the activity in the orbitofrontal cortex also tracks the ratings of the subjective experience of amphetamine (Völlm *et al.* 2004). Studies from other research groups have similarly shown that sex and stimulants like opium, cocaine and amphetamine also give rise to activity in the same brain regions as food, but to a stronger degree. However, this stronger activation does not necessarily mean that people would choose drugs and sex over food and drink if faced with starvation. Instead it suggests that drugs and sex are using the same reward circuits as food (Kringelbach 2004).

5.2 *Pain*

It is interesting to compare pleasure with another type of subjective experience, pain. Pain is a good example to study negative affective processing, especially since it is always defined subjectively. Its primary sensory representation is well understood; its reward circuits and autonomic connections are evolutionarily old and therefore likely to be consistent between individuals; it dominates sensory attention and so produces a clearly recordable conscious response; yet the subjective emotional experience of the same painful stimulus may be radically different between individuals. It is only recently that we have gained better insight into the workings of pain and pain relief (which can be, itself, pleasurable). We were able to shed further light on the basis of this subjective hedonic experience by making observations of the brain in two patients who suffered from chronic pain.

Both patients had undergone implantation of a deep brain stimulator to treat their intractable pain. We used MEG to map the changes in brain activity caused by the stimulation. When the stimulator was turned on, the first patient reported a significant decrease in his subjective pain. During these periods of pain relief we found corresponding significant changes in brain activity in a network that comprises the

regions of the emotional brain and includes the mid-anterior orbitofrontal and subgenual cingulate cortices (see figure 3A) (Kringelbach *et al*. 2007). The second patient no longer experienced pain even when his stimulator was turned off. As well as the orbitofrontal activity found in the previous patient, we also observed activation of the periaquaductal grey in this patient (Ray *et al*. 2007). This is one of the areas found to relieve chonic pain when stimulated in animal models. Human studies using fMRI suggest that this area is active when people are anticipating, but not yet experiencing pain (Fairhurst *et al*. 2007). We have used DTI to map some of the connections between these affective brain regions (see figure 3B) (Owen *et al*. 2007). Using further MEG experiments we aim to uncover the mediating factors that determine which of the many affective responses to pain such as flight, adaptation, avoidance are expressed.

5.3 *A model of affective processing*

The results of neuroimaging work from our group and others suggest a model (see figure 4) of affective processing within the area known as the orbitofrontal cortex (Kringelbach 2004, 2005). The orbitofrontal cortex is an area of the brain that receives inputs from all five classic sensory modalities: gustatory, olfactory, somatosensory, auditory and visual (Carmichael and Price 1995). It also receives autonomic sensory information. All this input makes the orbitofrontal cortex one of the most polymodal regions in the entire cortical mantle.

This model is obviously simplified but begins to address the basic principles of how food consumption and pain are controlled in the human brain. More research into the cortical mechanisms of food intake and chronic pain is likely not only to further elucidate the workings of this network but may perhaps also prove important to larger questions such as whether this is a generic network for other subjective experiences.

6. Artistic representations

Biomedical imaging allows us to map the structure and function of the human body and produce theoretical scientific models. The detail in these representations is the result of a multitude of choices, as segmentation and thresholds are selected during the data

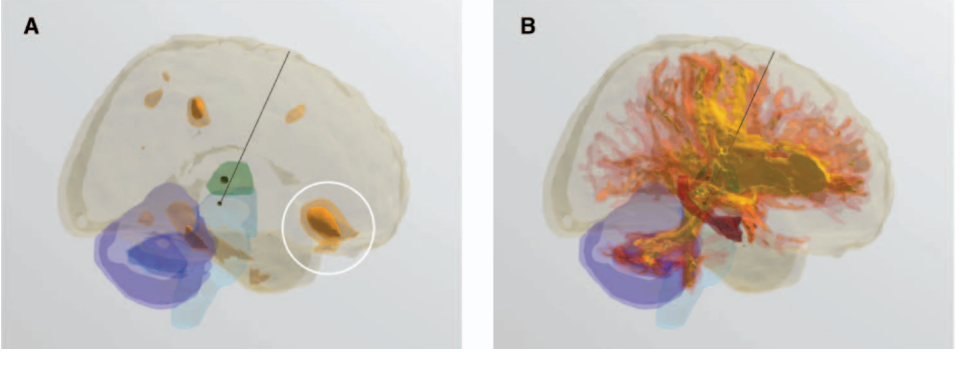

Figure 3. *Multimodality neuroimaging to understand pain*. (A) 3D reconstructed MEG data showing the areas of brain activation when a deep brain stimulator is turned on. The circled area is the orbitofrontal cortex. (B) 3D reconstructed DTI image showing the areas of the brain connected to the region stimulated.

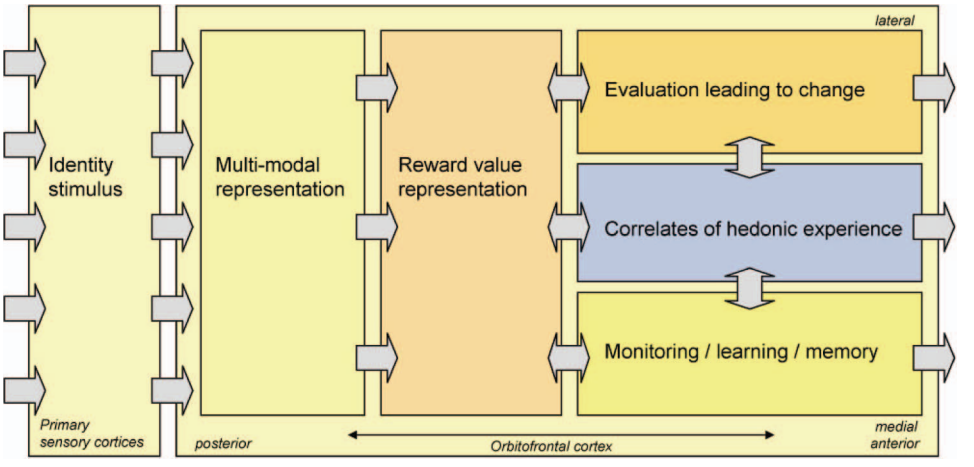

Figure 4. *Proposed model for the interaction between sensory and hedonic systems in the human brain using one hemisphere of the orbitofrontal cortex as an example*. Information is flowing from the left to the right of the figure. Sensory information is sent from the periphery to the primary sensory cortices, where the stimulus identity is decoded into stable cortical representations. This information is then conveyed for further multimodal integration in brain structures in the posterior parts of the orbitofrontal cortex. The reward value of the stimulus is assigned in more anterior parts of the orbitofrontal cortex from where it can then be used for influencing subsequent behaviour (in lateral parts of the anterior orbitofrontal cortex), stored for learning (medial parts of the anterior orbitofrontal cortex) and made available for subjective hedonic experience (mid-anterior orbitofrontal cortex). The reward value and thus also the subjective hedonic experience of a stimulus can be modulated by internal states, while the identity representations in primary sensory cortices are remarkably stable and not subjected to modulation. It should be noted that there is, of course, important reciprocal information flowing between the anterior regions of the orbitofrontal cortex.

processing. These choices when led by scientists are usually based on convention and experience. Instead, involving the unconventional sensibilities and intuitions of artists can produce novel visualizations and representations.

The artworks of the artist Annie Cattrell are good examples of such representations, which began by using fMRI to map the areas of the brain responsible for the neural processing of each of the conventional five senses (figure 2). This data was then used as the basis for a set of five rapid prototyped sculptures representing what is perhaps best described as 21st century portraiture (Kemp 2003). This piece entitled SENSE (see figure 5) was recently purchased for the Wellcome Trust's permanent collection.

It has been proposed that a hallmark of successful portraiture is that which informs us not only of the physical attributes of the sitter but also of the emotional qualities of both the sitter and the artist. Emotional likeness is an elusive quality. We are revisiting these issues in a contemporary setting by using biomedical imaging to obtain novel anatomical and functional information about the sitter. In particular we have investigated the affective experience of the sitter and are exploring ways to represent this information in virtual and physical sculptures. It is hoped these will provide a broader public understanding of neuroscience and may lead to novel insights.

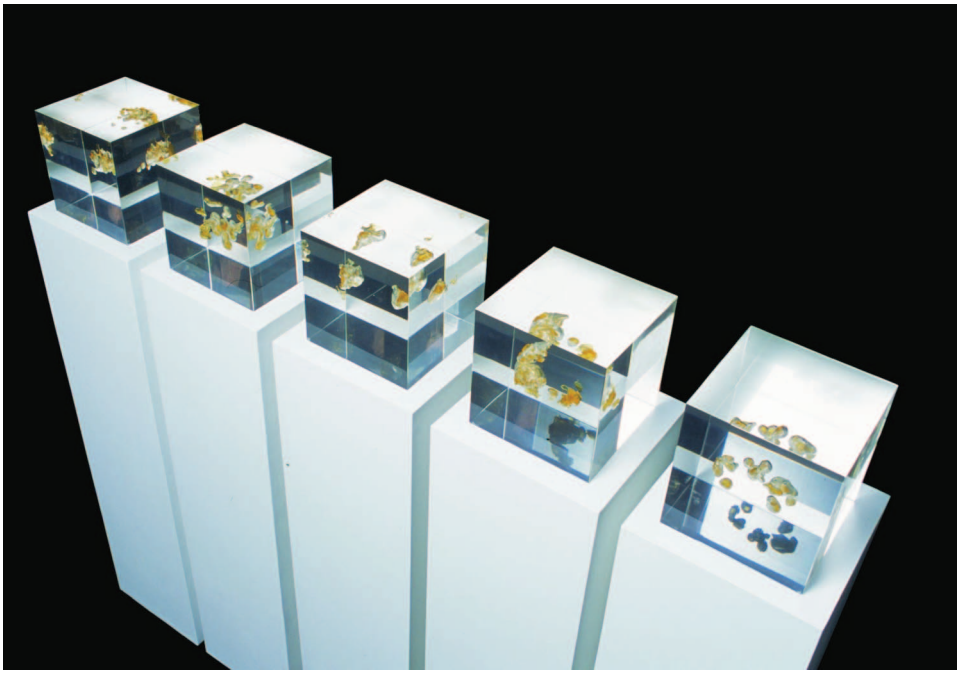

Figure 5. *SENSE by Annie Cattrell*. Sculptures of the five senses in a living person. (Photo: Peter Cattrell.)

7. Conclusion

The integration of natural sciences with art and cultural sciences to produce a human science centered model for design has been proposed by Professor Harada at Tsukuba University, Japan (Childs *et al*. 2002). Neuroimaging is the tool pivotal to making these collaborations beneficial.

To scientifically assess the human affective responses to design we need to quantify these experiences. New imaging technologies are opening the door to exciting investigations measuring real time changes in affect when subjects are presented with different stimuli.

These techniques are available and accessible. The information they provide is available to researchers from all disciplines. Neuroscientists can work with designers and developers to create new paradigms to investigate affective processing. These mutually beneficial collaborations provide ways of objectively assessing the affective impact of a design and by broadening the study of affective experiences perhaps bringing neuroscientists closer to producing models of human consciousness.

Finally we have shown that by combining the fields of contemporary sculpture, rapid prototyping and biomedical imaging we can also produce exciting new artistic representations to understand the complexities of neuroscience.

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