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Book Review

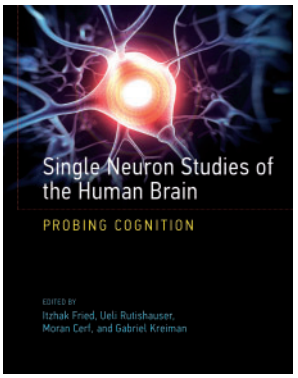
The neuronal representation of information in the human brain

The responses of single neurons provide evidence that is essential to understanding what information is encoded in a brain area, and how it is encoded, for the information conveyed by a single neuron is almost independent of that conveyed by others in the same population. The differences in the firing rate response profiles of single neurons to a set of stimuli or events encode most of the information about that stimulus or event. The representation is sparsely distributed, with neurons often having an approximately exponential firing rate distribution, with high firing rates to a few stimuli, and smaller and smaller responses to other stimuli in the set, and no response to most of the stimuli. It is in this way that information about particular stimuli is represented. For example, in the inferior temporal visual cortex, neurons encode in this manner which particular face or object is being shown (Rolls and Treves, 2011).

Evidence of this type is crucial to understanding the operation of the brain, for by reading the code from different connected brain areas, it is possible to start to understand what is being performed (or computed) by each brain region. This in turn is important for understanding neurological and psychiatric disorders and their symptoms, and for suggesting treatments based on what each brain region is performing, and developing hypotheses about how each cortical area operates (Rolls, 2008, 2016).

Much of the evidence on what is represented in different cortical areas comes from single neuron studies in macaques, including concepts about the roles of cortical areas that correspond to those in humans. The book *Single Neuron Studies of the Human Brain - Probing Cognition* edited by Fried, Rutishauser, Cerf and Kreiman is therefore important, for it reviews what is now being discovered from recordings from single neurons in humans, performed as part of a programme of clinical treatment, and even a little evidence of this type may help to show how the detailed studies in the non-human primate cortex are providing evidence that is relevant to understanding the human brain, and potentially its disorders.

SINGLE NEURON STUDIES OF THE HUMAN BRAIN - PROBING COGNITION
Eds. I. Fried, U. Rutishauser, M. Cerf and G. Kreiman, 2014
The MIT Press: Cambridge Massachusetts and London, England.
ISBN: 978-0-262-02720-5.
Price: £41.95.



The book has an important chapter by Adam Mamelak on the ethical and practical considerations for microelectrode recording studies in humans, pointing out that they may be useful, for example in assessing whether a brain area being considered for resection is operating pathologically or not, and for example in locating sites for possible deep brain stimulation by using the types of neuronal activity being recorded as markers. During the course of clinical investigations of this type some evidence about neuronal activity may become available, but of course there are many provisos that apply, such as that the brain region from which recordings are made may be dysfunctional, and that the time for recording from neurons is necessarily limited, so that the data obtained are likely to be limited.

Given these constraints, what findings are being made from single neuron recordings in humans?

Some of the most fascinating findings are about how neurons respond in medial temporal lobe regions. In Chapter 8 Mormann, Ison, Quiroga, Koch, Fried and Kreiman describe some neurons with responses that appear quite selective, with one neuron responding for example to Jennifer Aniston but much less to other individuals, and responding multimodally, for example not just to the sight of Jennifer Aniston, but also to the sound of her

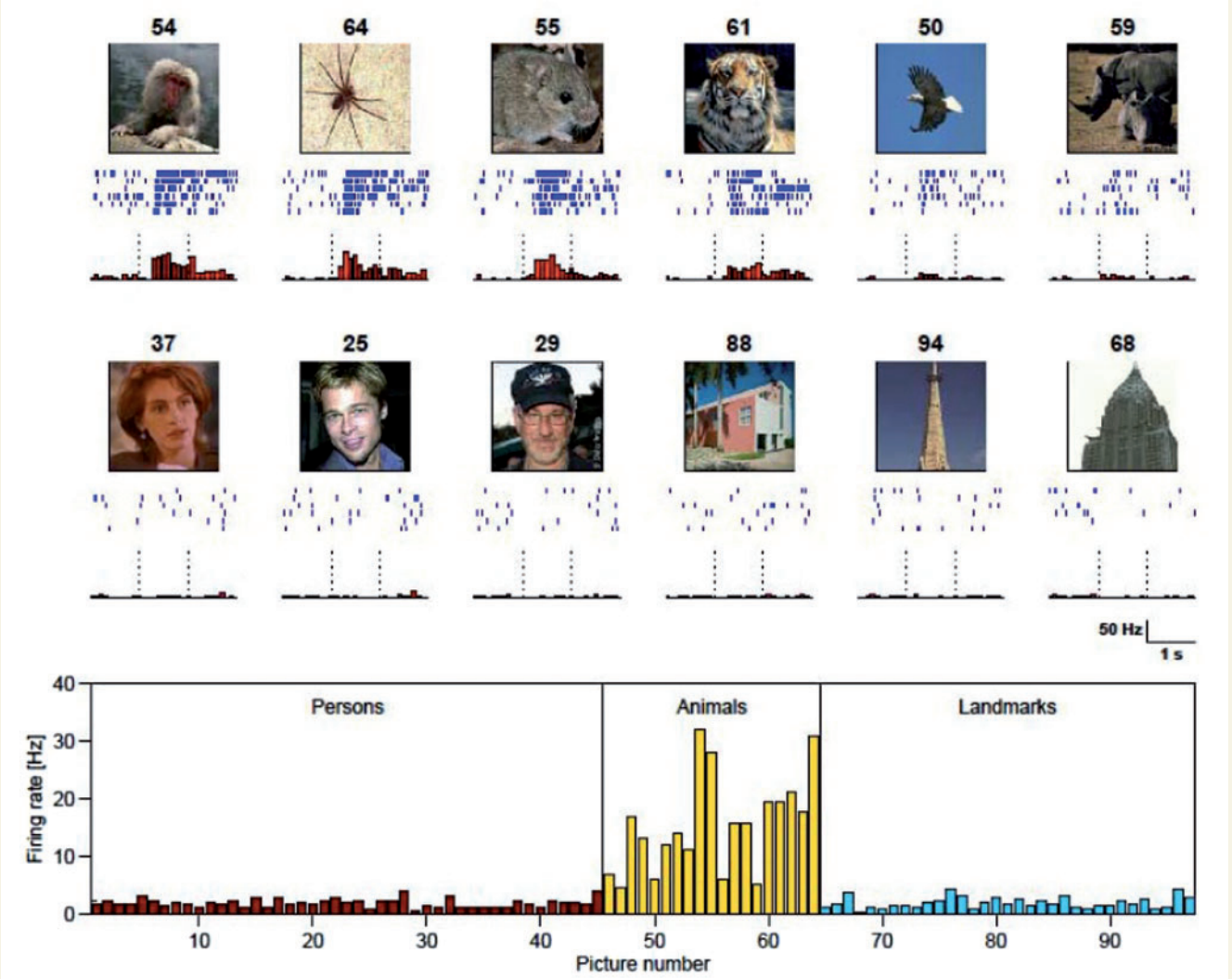


Figure 1 Example of a single neuron in the human amygdala activated by animal pictures. The neuron responded to different extents to pictures of animals, but showed no responses to pictures of humans or landmarks. *Upper rows:* Responses of a neuron in the right amygdala to pictures from different stimulus categories, presented in randomized order. For each picture, the corresponding raster plots (order of trials from top to bottom) and peri-stimulus time histograms are given. Vertical dashed lines indicate image onset and offset (1 s apart). *Lower row:* The mean response firing rates of this neuron between image onset and offset across six presentations for all individual pictures. Pictures of persons, animals and landmarks are denoted by brown, yellow and cyan bars, respectively. Reprinted with permission from Mormann *et al.* (2011).

voice. At first, the tuning of single neurons might on the basis of a few striking examples in humans, be thought to be more selective than those in the macaque temporal lobe, but on the basis of many such recordings, those who have recorded these neurons argue that the code is sparsely distributed (Chapter 8) (Quiroga *et al.*, 2008; Quiroga, 2012, 2013), and therefore somewhat similar to that of neurons in macaques (Rolls and Treves, 2011). To illustrate the type of tuning that can be found, the responses of a single neuron in the human amygdala activated by animal pictures are shown in Fig. 1. The neuron responded to different extents to pictures of animals, but showed no responses to pictures of humans or landmarks (Mormann *et al.*, 2011).

Neurons recorded in the human medial temporal lobe areas such as the hippocampus, are described as being 'concept neurons', for not only are they multimodal, but they can also respond to imagery of for example Jennifer Aniston, as in one famous case (Chapter 8). How does this fit in with concepts of hippocampal function? The hippocampus is thought to be involved in episodic or event memory, for example the memory of a particular person in a particular place (Rolls, 2008). Each memory must be as separate as possible from other memories, and the evidence is that single neurons in the macaque CA3 respond to combinations of, for example, a particular place being viewed, or a particular object, or a combination of these (Rolls *et al.*, 2005). Indeed the theory is that the

CA3 region with its recurrent collateral associatively modifiable synaptic connections enables any object or person to be associated with any place by this associativity, to form a unique episodic memory (Rolls, 1989, 2008; Kesner and Rolls, 2015). Human neurons in the hippocampus that respond to 'concepts', for example with quite selective tuning for a person, appear to be consistent with this theory. Of course, the nature of the sparsely distributed encoding is that no single neuron does need to be selective for just one person or object, for it is across a population of such neurons with sparsely distributed encoding that a particular individual is represented (Rolls and Treves, 2011) and becomes part of the autoassociation or attractor memory of a particular object or person in a particular place (Rolls, 2008; Kesner and Rolls, 2015).

Chapter 9 by Suthana and Fried considers the representation of space by neurons in the human medial temporal lobe. A potentially important difference between rodents and primates including humans, is that rat hippocampal neurons represent the place where the rat is located (O'Keefe, 1979), whereas a population of neurons in the macaque hippocampus and parahippocampal cortex has been discovered that represents a spatial view of a scene with its landmarks independently of the place at which the macaque is located (Rolls and O'Mara, 1995; Rolls *et al.*, 1997, 1998). Further, this representation is allocentric, in that it is the allocentric location in space being viewed and not egocentric cues such as eye position, or position relative to head direction, or indeed head direction itself (Georges-François *et al.*, 1999). The importance of these neurons is that they provide a basis for remembering where an object is located at a place at which one has never been present, such as a source of food at some distance away, or the position of a particular player when a goal was scored while one was a spectator who had never been on the pitch. Place cells could not implement that type of memory. The implication is that such spatial view cells are therefore very important in hippocampally mediated episodic memory in humans, of for example an object or person and where the object or person is located in space. What then is found in humans? It has been reported that in humans there are landmark (or spatial view) cells, as well as place cells (Ekstrom *et al.*, 2003), and further that some neurons do become activated during the recall of an episodic memory of the place (Miller *et al.*, 2013), just as spatial view cells do in macaques when a location 'out there' in space is recalled from an object (Robertson *et al.*, 1998; Rolls *et al.*, 2005; Rolls and Xiang, 2006). Thus spatial view cells in humans may be essential for episodic memory involving what was present at places 'out there', and further investigation of them seems important, especially if possible in real spatial situations where place and spatial view can be unambiguously separated (Georges-François *et al.*, 1999), rather than in the more artificial virtual environments presented on a screen that are often used.

A possible difference between the human and non-human hippocampal systems is that in rodents and non-human primates there may effectively be one hippocampus because the CA3 neurons are so extensively connected between the two hemispheres (Rolls, 2008), whereas in humans, there may be separate CA3 networks in the two hemispheres, for the left hippocampal system specializes in language-based memories, whereas the right hippocampal system specializes in spatial memory (Banks *et al.*, 2012). The underlying computational reason for this is, that language does not operate by spatial locations, that is, humans do not use and need a word-place episodic memory (Rolls, 2008, 2016).

Chapter 13 by Adolphs, Kawasaki, Tuduscuic, Howard, Heller, Sutherling, Philpott, Ross, Mamelak and Rutishauser describes face-selective neurons in the human amygdala, which seem very similar to those discovered in macaques (Leonard *et al.*, 1985; Gothard *et al.*, 2007; Rolls, 2011).

A possible difference of single neurons in the human medial temporal lobe is that many seem to have rather low firing rate responses compared to those in macaques. However, the firing rates of neurons in different cortical areas are very different. In the inferior temporal visual cortex neurons with peak firing rates of 100 spikes/s to the most effective stimulus are common, whereas in the hippocampus neuronal responses have much lower firing rates, typically reaching a peak of 10–15 spikes/s to the most effective stimulus, from a spontaneous rate of less than 1 spike/s (Rolls and Xiang, 2006). Thus when interpreting temporal lobe recordings in humans, it is important to take into account as much as possible the recording site, because what neurons respond to, and how much they respond, differs greatly between cortical areas. In this context, any information, such as MNI coordinates of recorded single neurons in humans, is important information to provide, and moreover will help the single neuron studies to be related to the activations found in human imaging studies, which of course reflect the average activity of hundreds of thousands of neurons, so provide little evidence about how the information is encoded by the neurons.

What are unique to humans are the findings on neuronal responses related to human language, described in Chapter 14 by Ojemann. Many of these recordings were made in lateral temporal cortex, and not from areas that are essential for language. One interesting finding has been of single neurons that change their activity when naming objects in one language, but not in another language. This suggests that the neuronal networks for different languages may be at least partly separate in terms of how they operate. Another interesting finding is that some temporal lobe neurons are involved in perception, and others in production, and indeed neurons with mirror-like properties are described as being rare in the superior temporal lobe cortical areas. In a more recent study, Halgren, Cash and colleagues described in the left anterior superior temporal gyrus of a right-handed man that 45% of units robustly

fired to some spoken words with little or no response to pure tones, noise-vocoded speech, or environmental sounds (Chan *et al.*, 2014). The tuning to words might be described as sparsely distributed. Many units were tuned to complex but specific sets of phonemes, which were influenced by local context but invariant to speaker, and suppressed during self-produced speech. The firing of several units to specific visual letters was correlated with their response to the corresponding auditory phonemes, providing direct neural evidence for phonological recoding during reading. A fundamental issue is how syntax is encoded in the cortex. A recent hypothesis is that place coding might be used, with for example, a neuron responding to the word 'cat' when it is the subject of a sentence, and not when it is the object (Rolls and Deco, 2014). If this hypothesis was found to be the case in single neuron recordings in future, this would greatly simplify concepts about how language, and in particular syntax, are implemented in the cortex (Rolls and Deco, 2014; Rolls, 2016).

Other chapters of the book cover topics such as recording methods, the use of microelectrode recordings in deep brain stimulation surgery, single units for motor prostheses, and using the activity of single neurons to help understand epileptic seizure generation.

Overall, this is a very useful collection of chapters that provides reviews of an important source of evidence for understanding human brain function that has been collected during clinically relevant investigations. There are likely to be many further advances made in future single neuron recordings in humans, and this book provides an overview of what has been found already, which paves the way for future research in this area. It is reassuring that many of the findings are consistent with what has been discovered by single neuron recordings in non-human primates, from which many discoveries about what information is encoded in different cortical areas, how it is encoded, and the principles of operation of the cortex are being made (Rolls, 2008, 2016). It must be borne in mind that data of this type are obtained from human participants whose brains are being examined for clinical reasons, and this needs to be taken into account when considering the findings.

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