



## Editorial

## Brain, memory and development: The imprint of Gabriel Horn



Gabriel Horn in India in 1976. Photo courtesy of Lady Horn.

This special issue of Neuroscience & Biobehavioral Reviews is dedicated to the memory of Sir Gabriel Horn, who died on 2nd August 2012. In his impressive career that spanned more than 50 years (Bolhuis and Johnson, 2012; Brown, 2013), Horn's contributions to cognitive neuroscience consistently pioneered new approaches and areas of investigation for others to follow, as illustrated by the papers in this special tribute issue. The contributions to this issue have been inspired particularly by Gabriel's pioneering work on the neural mechanisms of learning and memory in imprinting.

As a medical student at the University of Birmingham, Gabriel already showed great interest in brain and cognition, and during a year working with Solly Zuckerman, Professor of Anatomy, he wrote an essay on 'The Neurological Basis of Thought' published in a student journal called 'The Mermaid' (Horn, 1952). In this paper, Horn laid the foundations of much of his later work on the neural basis of attention, habituation, memory, and development. Zuckerman immediately recognised the originality of the essay, and wrote 'Hebb' all over it. Donald Hebb had published his seminal book 'The Organization of Behavior' in 1949, outlining a theory of memory and neural connectivity, which remains a bible of cognitive neuroscience to this day (Hebb, 1949). Gabriel had never heard of Hebb's theory at the time, but had independently come up with some similar proposals in his student essay.

Gabriel Horn did seminal work on habituation and on cross-modal and attentional modulation of early sensory processing (Horn, 1985; Bolhuis, 2000; Bolhuis and Johnson, 2012; Brown, 2013), but perhaps his greatest achievement was his study of the neural mechanisms of learning and memory in imprinting. Thus,

for this special issue we decided to focus on the impact of Gabriel's work on the neural mechanisms of imprinting on contemporary work on brain, memory and development. After an introductory paper by Gabriel's long-standing collaborator and friend, Patrick Bateson, the contributions to this issue have been grouped according to the particular aspects with which they are concerned.

### 1. Memory and brain: localisation of the memory trace

Horn's work has been vitally important in the quest for the localisation of the memory trace. In the early 1970s, Horn's search for the ideal model system with which to study the basic mechanisms of memory led him to discussions with his Cambridge colleague, Patrick Bateson, and the biochemist, Steven Rose. This team built on the well-known attempts at localisation of the neural substrate of memory initiated by Karl Lashley in the 1950s, who went 'in search of the engram' – the 'mark' or 'trace' left in the brain by the learning experience (Lashley, 1950). Famously, Lashley became despondent with regard to the possibility of neural localisation of the memory trace. Horn and his colleagues took up the challenge through the analysis of a robust and replicable form of early learning seen in precocial birds: filial imprinting (Bateson, 2015).

Horn pioneered a 'bottom-up' approach to the study of memory. He argued that in order to be able to analyse the neuronal correlates of learning and memory, the researcher has to know where in the brain to look for these correlates. This was quite different from the dominant 'top-down' paradigms at the time, where a particular brain region, such as the hippocampus, or neural mechanism, such as long term potentiation (LTP) was simply assumed to be crucial for memory. Horn and collaborators took a completely different approach, their only presupposition being that learning and memory would involve some kind of structural change in the brain, in the way suggested by Hebb. Such a change was thought to involve protein synthesis. In the initial experiments the chick brain was quite simply subdivided into three main regions (midbrain, forebrain roof and forebrain base), where protein synthesis was measured in relation to the strength of learning. Gabriel's approach proved to be hugely successful: imprinting became the first paradigm where Lashley's dream of finding the engram was realised, although neural reality turned out to be somewhat more complicated than one might have initially imagined. Horn and collaborators established that the neuronal changes underlying imprinting were not widely distributed in the brain, but restricted to a few discrete brain

regions, including the intermediate and medial mesopallium (IMM) (Horn, 1985).

Malcolm Brown was a PhD student and postdoc with Gabriel, which inspired him to subsequently investigate the neural mechanisms of recognition memory in mammals, particularly the vexing issue of the localisation of the memory trace. Some of that work is summarised in Brown and Banks (2015). Barry Keverne was a colleague and friend of Gabriel's at Cambridge, and Director of the Sub-Department of Animal Behaviour when Gabriel's lab moved there in the late nineties. At Cambridge, Keverne was involved in a quest for the localisation of the neural substrate for olfactory memory, with his former PhD student Peter Brennan among others. Brennan and Keverne (2015) review some aspects of this work here. Johan Bolhuis was an undergraduate student and postdoctoral fellow with Gabriel. Inspired by Gabriel's imprinting paradigm, Bolhuis subsequently focussed his attention on the analysis of the neural substrate of birdsong learning and memory, with his former PhD student Sanne Moorman among others (Bolhuis and Gahr, 2006; Bolhuis et al., 2010). Bolhuis and Moorman (2015) provide an overview of recent efforts to localise the neural substrate of tutor song memory – often called the 'template' – including some fascinating parallels with filial imprinting.

## 2. Molecular and cellular mechanisms of memory

Having made major advances in localising the neural substrate of memory, Horn and collaborators investigated the changes that bring about alterations in connections between specific groups of neurons in learning and memory (Horn, 2004). Within the same model system (imprinting) an interdisciplinary and multi-method approach was applied using molecular, neurochemical, neuroanatomical, electrophysiological, and behavioural techniques. Gabriel's long-time collaborators Revaz Solomonina and Brian McCabe review the molecular mechanisms of memory during imprinting (Solomonina and McCabe, 2015; cf. Bateson, 2015).

Horn's work on imprinting exerted strong conceptual influence on research into the neural mechanisms of birdsong learning, conducted in avian species that learn their vocalisations from an adult model (Bolhuis and Moorman, 2015). Claudio Mello and David Clayton have been at the forefront of research into the molecular mechanisms underlying the memorisation and production of learned vocalisations in songbirds. Here they review the state of the art of large-scale molecular-genetic research in songbirds, focusing on work done in the zebra finch (Mello and Clayton, 2015).

Eddy van der Zee was a postdoc in Gabriel Horn's lab at Cambridge, where, in collaboration with Johan Bolhuis he investigated the role of kinases in imprinting. Here he reviews his work and that of others on the role of kinases in functional and morphological synaptic plasticity in learning and memory in mammals.

## 3. Neural systems analyses of learning and memory

During the search for the 'engram' in imprinting, Horn and collaborators discovered a number of important characteristics of memory at the neural systems level. One of the many fascinating aspects of their work on imprinting is that although neuronal changes consequent upon learning have been identified in both the left and right IMM, they are different in the two hemispheres (Horn, 2004). Similar accounts of hemispheric asymmetry have been reported in birdsong and in relation to human speech and language. Sanne Moorman and Alister Nicol (2015) – the latter a former postdoc and long-time collaborator of Gabriel Horn – provide an extensive overview of these remarkable parallels.

Most recently, Horn and colleagues focused their efforts on the role of sleep in learning during imprinting. In a landmark paper

in *Current Biology* (hailed as a major advance by Robert Stickgold (2008) in a later issue), they demonstrated that a period of sleep shortly after the imprinting episode is essential for memory consolidation (Jackson et al., 2008). This exciting new line of research is being pursued at Cambridge by Horn's long-time collaborators, Brian McCabe and Alister Nicol. Vorster and Born (2015) provide a wide-ranging review of the role of sleep in learning and memory in mammals, birds and invertebrates. In addition, Beckers and Rattenborg (2015) review current research in the neural analysis of sleep in birds, using sophisticated electrophysiological techniques.

In 2001 Horn and his colleagues (Horn et al., 2001) published an important paper, challenging the predominant view that the neural changes underlying memory reflect linear processes such as are implied in simple Hebbian models of memory-related neural plasticity. Cohen et al. (2015) discuss the issue of memory encoding and consolidation in a wider context.

## 4. Developmental plasticity and learning: lessons from imprinting

Gabriel Horn's classic work on imprinting has had wider implications for the study of learning and development in general. Robert Honey was a postdoctoral fellow with Horn and Bateson, investigating the nature of the learning processes in imprinting. Here, together with Montuori he reviews the wider topic of the formation of representations in learning and development (Montuori and Honey, 2015).

In the mid-1980s, Horn and collaborators discovered that the development of social preferences in chicks is a result, not only of learning (imprinting), but also of predispositions – perceptual preferences that develop in young animals without experience with the particular stimuli involved. Horn et al. found that, during development, specific predispositions interact with learning, resulting in particular social preferences. Further, Horn's group demonstrated that the two systems (predispositions and imprinting) have different neural and biochemical substrates. Horn's work on predispositions and imprinting has been widely influential on research into the early development of social behaviour in both animals and human infants. Mark Johnson, a PhD student of Horn's, went on to extend the two systems model to data from human infants and their identification of social and communicative partners (conspecifics; Johnson & Morton, 1991). Working with collaborators, including current co-authors Senju and Tomalski, he has marshalled evidence for a sub-cortical route for face and direct eye gaze detection that modulates activity in the human cortical social brain network (Johnson et al., 2015). Horn's foundational studies in this area have also been extended into two other related areas. First, Rosa Salva et al. (2015) review a range of other social predispositions toward animate creatures that Giorgio Vallortigara's group has discovered using the chick imprinting paradigm, and they speculate on the neural substrates of these systems. Second, and building on this work in typical development, several investigators have applied the general model to atypical developmental trajectories, such as the common neurodevelopmental disorder of autism. Klin et al. (2015) present a view of autism as a disturbance of the basic mechanisms of orienting toward the eyes of another, and draw parallels and inspiration from the earlier imprinting work pioneered by Horn. Rhiannon Meredith (2015), Brian McCabe's former PhD student at Cambridge, extends the notion of a sensitive period in development, and suggests that some human neurodevelopmental disorders such as autism may be best characterised in terms of disturbance to the basic mechanisms underlying such periods of plasticity.

Taken together, the contributions to this special issue show that Gabriel Horn's pioneering work has created an enduring legacy to

cognitive neuroscience. The rich diversity in the fields of research discussed in the different papers illustrates how Gabriel's work continues to inspire next generations in the study of brain, memory and development.

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