NEUROCHEMISTRY OF CONSCIOUSNESS: NEUROTRANSMITTERS IN MIND
Edited by E. Perry, H. Ashton and A. Young
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Of what relevance is the study of the neural correlates of consciousness to the practice of clinical neurology? Until recently, one answer to this question might reasonably have been ‘not much’, consciousness being largely taken for granted by neurologists except in those cases in which it was deemed ‘impaired’ or ‘reduced’, in which case steps to identify the cause(s) of impairment needed to be undertaken. Hence, the study of consciousness has largely been the preserve of philosophers, a domain of questions rather than answers (Dennett, 1996). However, neuroscientists have become increasingly interested in consciousness with the realization that its neural correlates, particularly electrophysiological and functional anatomical, might possibly be defined with existing research techniques (Zeman, 2001). The editors of this book, building on their known neuropharmacological interests (Perry et al., 1999), have sought to show that neurotransmitters may be central to the mechanisms of consciousness, by outlining the neurochemical mediators of distributed neural function and their relationship to various conscious states.

Conscious awareness may be described in terms of two components, one quantitative (‘level’), encompassing arousal, alertness, vigilance; the other qualitative (‘intensity’), encompassing selective attention and mental experience. A priori it would seem unlikely that any single neurotransmitter, or anatomical locus, could be identified with such diversity of function. In a brief introductory section on neurotransmitter systems, the neuromodulatory functions of the cholinergic system, which encompasses divergent and convergent projections from basal forebrain and brainstem pedunculopontine nuclei to thalamus and cortex, are emphasized as an anatomical arrangement well suited to mediating distributed neural function and hence conscious activity.

The three main sections of the text detail the function (or dysfunction) of neurotransmitter systems in natural, drug-induced and brain pathological states associated with changes in consciousness. Natural alterations of consciousness include attention, memory, motivation and sleep. Considering attention, itself a distributed and fractionable function, the currently available evidence suggests a role for noradrenaline in alerting/arousal, whereas acetylcholine may control selective attention. Studies of the neurochemical modulation of learning and memory also indicate roles for cholinergic systems but it has proven difficult to show that cholinergic modulation can exclusively affect memory functions. For example, the effects of cholinesterase inhibitors (ChEIs) in Alzheimer’s disease seem largely attentional rather than mnemonic. Bound up with learning and memory are the brain reward and punishment systems, central to motivation, which are influenced by complex interactions of many neurotransmitters.

Understanding the neurochemistry of sleep, dreaming and the effects of drugs on the sleep–wake cycle, is suggested to be critical to understanding the neurotransmitter correlates of consciousness. The neurochemical changes which trigger natural sleep, and distinguish REM from non-REM sleep, are held to argue strongly in favour of a role for altered neurotransmitter activity in conscious awareness. The role of adenosine as a sleep-inducing factor suggests its possible candidacy in mediating altered states of consciousness. Therapeutic implications follow from a consideration of parasomnias, arousal disorders arising from non-REM sleep, as having a neurochemical basis (e.g. serotonin reuptake inhibitors for sleep terrors). Likewise, cholinergic deficits are suggested to be critical to the (often neglected) sleep disturbances in neurodegenerative diseases such as Parkinson’s disease, dementia with Lewy bodies (DLB) and Alzheimer’s disease (‘sundowning’).

As well as hypnotics, other drug-induced alterations of consciousness are considered, specifically the use of neuroleptics and general anaesthetics. The relevance of neuroleptics to consciousness rests on clinical phenomena such as the neuroleptic malignant syndrome (which may also occur with non-neuroleptic medications), and severe neuroleptic sensitivity reactions, occurring for example in DLB. Dopaminergic blockade is suggested to be the common denominator here, although other neurotransmitters may also

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be implicated. General anaesthetic agents, on the other hand, are clearly not alike in the way they alter consciousness, different agents acting on different synaptic pathways within the neural networks that underlie alertness, learning and memory. This may result in qualitatively different states: for example, ketamine, which unlike many other anaesthetics does not potentiate GABA_\text{A} receptors, induces an inattentiveness to surroundings rather than unconsciousness, perhaps through actions on NMDA and nicotinic receptors.

The quality of consciousness may be described not only in terms of attentional states, but also by the content of the conscious state. In this context, the neurochemistry of delirium and hallucinations is a subject of particular interest, in view of the well-recognised propensity of certain drugs to induce these states. The pharmacological heterogeneity of these drugs makes it difficult to infer common neurochemical pathways, but nonetheless roles for cholinergic deficiency and dopamine excess are suggested, with possible modulation by serotoninergic pathways. The pharmacology of plant chemicals, used in many cultures to induce altered states of awareness, is again heterogeneous but monoaminergic and cholinergic mechanisms seem most commonly implicated.

Alterations of consciousness as a consequence of pathological changes within the brain are addressed in the final section, covering neurodegenerative disorders, schizophrenia, mood disorders, mental retardation and autism. Such conditions present the challenge of disentangling effects on conscious awareness from other effects of transmitter disturbance. DLB may be particularly significant in this respect, the fluctuating level of cognitive abilities resulting from an ‘unstable platform of consciousness’, which may largely be due to cholinergic abnormalities, themselves potentially amenable to treatment (e.g. with ChEIs).

Neurologists who may previously have shied away from the subject of consciousness, perhaps alienated by seemingly esoteric issues, for example the laws of qualia (elucidated by Ramachandran and Blakeslee, 1998), will find nothing so alarming in this book. This book might be described as reductionism ‘pure and simple’: conscious awareness is assumed to be a functional property of the human brain (p. xi). There is no debate about thorny issues, such as whether the brain can be held to mediate consciousness (e.g. Tallis, 2000). (I presume these may be tackled in other volumes of the Advances in Consciousness Research series, to which this book belongs: dating back to 1995, 41 volumes are already published or in preparation.) Nor is there much discussion of binding mechanisms underlying consciousness, or of correlations between neurotransmitter and other neural correlates of consciousness. Having mentioned (p. 26, 35–38) the Hameroff–Penrose orchestrated objective reduction model of consciousness, and its relationship to microtubular function, it would perhaps have been interesting to read some speculations as to how this might relate to the clinical phenomenology of dementia syndromes, which may be conceived of as disorders of cytoskeletal microtubular function.

How might the editors carry their argument further, accepting the assumptions that consciousness is a function of brain and that pathological alterations in function can shed light on physiology? From the physiological perspective, it would perhaps be interesting to attempt to relate the neurochemistry of the visual cortex to previously elaborated theories of visual consciousness (e.g. Zeki and Bartels, 1999). From the pathological perspective, the neurochemistry of other clinical conditions in which consciousness is altered might be covered: coma is acknowledged to be an omission, but it might also be worth exploring the neuropharmacology of persistent vegetative states, akinetic mutism and abulia, as well as clinically similar states in which consciousness is not impaired, such as the locked-in syndrome (a double dissociation?). And what about epileptic syndromes, possibly the commonest pathological cause of altered states of consciousness?

In an ‘envoi’, the editors admit they were uncertain of the outcome when the authors were first invited to contribute to the book. The resulting volume may not greatly influence current neurological practice, but by suggesting altered neurotransmitter function may underpin states of altered consciousness it does hold out the hope that these may eventually be amenable to pharmacotherapy. It also has the merit of clearly demonstrating the significant overlap, and hence the artificiality of distinctions, between areas traditionally deemed neurological and psychiatric, organic or non-organic. Overall, I found this a stimulating book and look forward to a second edition in due course, hopefully free of the irritatingly frequent typographical errors, with a more thorough index, and including a listing of authors and their affiliations.

A. J. Larner
Walton Centre for Neurology and Neurosurgery, Liverpool, UK

References