MEETING REPORT

Behaviour, brain systems and pharmacology*

The 2007 meeting of the European Behavioural Pharmacology Society (EBPS) was more international than its name suggests. With 29 countries represented, its significance seemed more than just confined to Europe. There was a heady mix of plenary lectures, parallel symposia and poster sessions that spanned three days and its flair was truly international with participants and speakers from the Americas, Europe, Asia and Australia. The meeting was about behaviour, the brain systems and pharmacology involved, and ranged from broad concepts to basic mechanisms.

The plenary lectures set the tone for the themes of the meeting that spanned the realm of neurodegenerative diseases, psychotic disorders, addiction, obesity, cognition, learning and memory, and social behaviour from clinical to neurobiological to pharmacological and molecular biological aspects. Jane Stewart (Centre for Studies in Behavioural Neurobiology, Concordia University, Montreal, Canada) in her plenary lecture spoke on drug use and relapse with specific reference to her decades-long research in cocaine and what directions the development of drug treatments should take. She dwelt at length not only on cocaine, but also on heroin and opium, and discussed mechanisms that underlie acquisition of drug preference to habituation or addiction, the phases involved and relapse. The new direction she gave based on her recent research was how abstinence could be molecularly targetted to produce inhibition of the habituated response to the stimulus. Ferdinando Nicoletti (Department of Human Physiology and Pharmacology, University of Rome, Italy) spoke at length on the whole spectrum of metabotropic glutamate receptors in the central nervous system and elsewhere, and mentioned specifically their significance in tumour growth.

The role of metabotrophic glutamate receptors was the theme of the first symposium. Their activity is modulated by dopamine, and this mechanism appears to underlie the impaired behavioural inhibition in schizophrenia studied using acoustic startle habituation deficit. The role of dopamine D1 and D2 receptors in excessive incentive learning models in rats was dealt with, and also how their blockade could be used in the development of suitable treatments. All presently available drugs seem to have a lack of efficacy against negative symptoms and cognitive deficits in neurodegenerative and psychotic disorders. Typical antipsychotic drugs act via blockade of striatal dopamine, while atypical ones show a preferential affinity for serotonin receptors. The direction that the development of present drugs is taking include agonism of serotonin $5HT_{-1A}$ receptors and/or antagonism at dopamine D2 receptors.

One symposium was devoted to proposals for possible drugs to treat various nervous disorders that lead to cognitive deficits and anhedonia, seen in neurodegenerative and psychotic disorders. One possible directive again is to combine treatment by administering dopamine D2 and serotonin $5HT_{-1A}$ receptors leading to lesser cognitive deficits. Selective dopamine D3 receptor antagonists also appear not only to reduce cognitive deficits but also anhedonia. The neurokinin receptor was suggested as another possible site for the action of these drugs; it influences dopaminergic transmission, and knockouts demonstrate enhanced cognition. Another strategy suggested was the use of dopamingeric stabilizers.

The next symposium dealt with forward and reverse genetic approaches using knockouts to understand the underlying mechanism of addiction. Neurobehavioural mechanisms underlying drug addiction and obesity was another theme. While behavioural sensitization, wherein the stimulus gains salience through repeated exposure, is the same in both drug addiction and obesity, neural mechanisms seem to differ, or may be not? Both are similar in that both target dopamine transmission. However, they are also different, since the dopamine response to food undergoes a single-trial, motivational and slowly reversible habituation, while response to drugs is resistant to habituation reversal. This appears to be largely because of the mechanistic differences in dopamine action on neurons in nucleus accumbens shell and the prefrontal cortex.

One symposium focussed on the hypothalamus and neuropeptides, with particular reference to the lateral hypothalamus as the neural substrate for reward. Implicated neuropeptides are orexin and melanin concentrating hormone which are found to be crucial in integrating hypothalamic centres with mesolimbic dopaminergic systems.

Another symposium was dedicated to the psychopharmacology of phosphodiesterase (PDE) inhibitors in enhanced cognition and memory in general. PDEs form an integral part of the dopamine D1 and D2 expressing pathways in the striatum. In neural disorders with cognitive dysfunction, PDE inhibitors could be used as a receptor-independent approach to treatment. PDE inhibitors of classes PDE2 and PDE5 can be used as memory-enhancement drug complements. Even generally, PDE inhibitors may have great potential as memory-enhancing drugs acting via the cGMP and cAMP pathways in neurons by preventing its breakdown. Another class of PDEs, namely PDE4 class shows antidepressant activity.

Memory impairers such as cannabis too got attention. Cannabis addicts normally show impairments in memory formation. Cannabinoid receptors in hippocampus have been implicated in memory processing, be it spatial memory, or they are known to modulate short-term memory. Long-term use of cannabis leads to risk of schizophrenia by precipitating the disorder in genetically vulnerable individuals. Cannabinoids are also known to inhibit sociality.

A symposium was devoted to pain, by giving an overview of the underlying mechanisms, symptoms and treatment options. It brought out the gap that exists between fundamental research and the limited number of novel pain-killers. Research has primarily focused on somatic structures, but there also exists an affec-

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tive component to pain, for which the search in on for animal models.

Another symposium zeroed in on the discussion about behavioural guidance by predicted reward. The prediction of future events based on ongoing sensory processing constitutes basic brain computing. A stimulus, when repeatedly paired with a reinforcer, can promote goal-directed behaviour. The protagonists here are the dopaminergic neurons, the stage for the acquisition being the nucleus accumbens and the prefrontal cortex. The processing is phasic with activation of dopaminergic neurons by cues that predict reward. The acquisition pathway seems to differ from the habit pathway, with the latter involving the striatum. Various drugs of abuse, e.g. cocaine addiction, have revealed this dissociation between acquisition of the behaviour guided by predicted reward and its transition to the striatal habituation pathway.

A symposium was devoted to translational medicine in brain research and covered the whole spectrum of translational models of cognitive function, and detailed how models, including behavioural and knockout models of depression and anxiety can be used for drug discovery and development.

Food-seeking in obese people and other obsessive compulsive disorders and the influence of dopamine D2 and kappa opioid receptors were also dealt with. The meeting had much mention of receptor types and sub-types, agonists, antagonists and inverse agonists, showing just how fast the field of neuropharmacology advances and how complex it can get. Pharmacokinetics of these substances, be it neurotransmitters, their agonists, antagonists and inverse agonists and drugs, and possible transport mechanisms through the blood–brain barrier were also discussed.

The symposium on social behaviour with particular reference to neurotransmitter–receptor systems and their role in animal–animal interactions received particular attention. The role of mu opioid systems and their involvement in mother–pup interactions in rodents was discussed, the model used being mu knockout mice. Opioid systems influence social behaviour; morphine, an agonist reduces affiliation, while naloxone an antagonist increases social affiliation. The involvement of the dopamine system in social attachment in male–female interactions and pair-bonding and male–male interactions in voles formed an interesting talk. Dopamine D1 activation impairs bonding, while D2 activation enhances it. The role of inhibitory neurotransmitter GABA and GABA–serotonin interactions in aggression behaviour, particularly in those elicited by alcohol were dealt with. The molecular biology of aggression has thus far not been able to identify genes for aggressiveness. What is proven is that low serotonin levels lead to aggression, serotonin transmission in alcoholic models of mice seem to occur in 'bursts', with serotonin agonists reducing aggression; positive modulation of GABA receptors, on the other hand, increase aggression. The story, however, gets more complicated when one considers monoaminergic crosstalk and feedback control not only by excitatory glutamate and GABA, but also by modulatory neuropeptides. The psychopharmacology of play behaviour in adolescent rats was also discussed.

To complement these symposia there were poster sessions on the themes Parkinson's, Alzheimer's, schizophrenia, anxiety, depression, stress, addiction, cognition, learning and memory – using drugs, agonists, antagonists, inverse agonists, knockout models, behavioural models from the academia and from the industry. In all, as the themes of the symposia indicate, there was a nice blend of industry and academia, with the approach throughout being both clinical as well as neuropharmacological. This effort of the EBPS highlighted the advances in the field thus far, and emphasized on what possible directions future research in neuropsychopharmacology and future drug development for treatments should take.

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MEETING REPORT

Seminar on male infertility*

In our overpopulated country, the presence of infertility, its increasing trend and its clinical management come as a surprise to some. The healthcare system in India is characterized by multiple systems of medicine, mixed ownership patterns and different kinds of delivery structures. People with infertility problems should have immediate access to an integrated multidisciplinary service that provides efficient and accurate assessment of the clinical situation. This should lead to individualized management founded on evidence-based principles of care. It should be reinforced by access to adequate information, appropriate counselling services, and ethical and cultural considerations. At all times, the infertile couple should be treated with respect, and supported in making informed choices about their care and management.

India is emerging as the most favoured destination for medical tourism. This is because of its infrastructure and technology, which are on par with those in USA, UK and Europe. India has some of the best hospitals and low-cost treatment centres in the world, providing the best facilities. To establish India in a leading position in the global infertility treatment, a holistic approach to the management of infertility is a must. To look at the advances in infertility diagnosis and treatment in ayurveda, allopathy, unani-tibb, siddha and homeopathy, a national seminar on male infertility was organized recently. There were 160 participants from different institutes of India.

Shrishailesh Amarkhed (J. N. Medical College, Belgaum) in his inaugural address spoke on current understanding of the male reproductive system, endocrinelogy and spermatogenesis. Vaidya Pawan-

*A report on 'VRISHYA 07 – A National Seminar on Male Infertility' held at Shri B.M.K. Ayurveda Mahavidyalaya and Hospital, Belgaum during 26–27 October 2007.