FONDATION IPSEN

POUR LA RECHERCHE THÉRAPEUTIQUE

Press release

Seventh *Colloque Médecine et Recherche* of *La Fondation Ipsen* in the Endocrinology series: "Hormones and Social Behaviour"

Paris (France), 4 December 2007 – Aggression, fear, social bonding, sexual behaviour, child abuse and autism were discussed yesterday at the seventh *Colloque* of *La Fondation Ipsen* devoted to endocrinology. At this meeting, leading scientists from Europe and the U.S. presented their latest results and discussed ideas on how hormones regulate the cellular and neural mechanisms that underlie the behavioural and psychological aspects of social behaviour. The hormonal influences on social behaviour have far reaching effects and consequences.

Hormones play a significant role in causing fear, aggression and sexual behaviour but the extent and complexity of the hormonal input into these and other socially relevant behaviours are only now becoming apparent. Also being explored is the impact that hormonal imbalances have on mental health regulatory systems. This Paris-based meeting was organised by Donald Pfaff (*The Rockefeller University, New York*), Philippe Chanson (*Hôpital Bicêtre, Paris*), Claude Kordon (*Institut Necker, Paris*) and Yves Christen (Fondation Ipsen, Paris).

Research in the past 20 years has broadened the concept of what a hormone is from a molecule with a few, well-defined targets and effects, to one with a range of subtle actions and complex interactions. The same molecule that acts as a classic hormone in the body may modulate synaptic transmission in neural circuits or even act as a neurotransmitter. The effects of hormones are now known to range from physiological and behavioural homeostasis, to regulation of mood, promotion of certain emotional states and the furtherance of inter-personal interactions.

One example of the various effects hormones can have on the body that was discussed extensively at the meeting was oxytocin, which regulates parturition and milk production and is also involved in promoting trust, maternal behaviour, social recognition and bonding (Ernst Fehr, *University of Zurich, Switzerland*; Inga Neumann, *University of Regensburg, Germany*; Pfaff; Larry Young, *Emory University School of Medicine, Altanta, USA*). Oxytocin and its close relative, vasopressin, have become known as "feel-good" hormones that promote calm and reduce stress and anxiety. One action of oxytocin seems to be to reduce the activity in the circuits involved in processing fearful stimuli in a part of the limbic system of the brain that regulates feelings and emotions (Fehr). The effects of oxytocin may be counteracted by a priming input to this area that comes from the general arousal system located in the brain stem and promotes social anxiety (Pfaff). The oxytocin-producing neurons in the hypothalamus, the hormone-regulation centre of the brain, respond to demand by short-term changes in both structure and function, indicating a high degree of tuning in this sensitive system (Dionysia Theodosis, *Inserm U378, Bordeaux, France*).

A significant regulator of aggressive behaviour is the neuromodulator, serotonin, also known as 5-hydroxytryptamine (5HT). Although 5HT is important in many brain circuits, the

specificity of its action is determined by the selection of the 14 known types of 5HT receptor carried by particular neurons. The configuration of 5HT receptors on both pre- and post-synaptic neurons that is involved in aggressive behaviour in mice is being determined by a combination of genetic and pharmacological manipulation, revealing a highly complex regulatory system (Bernend Olivier, *Utrecht University, The Netherlands*).

Sex hormones play very important roles in the body. The role of androgens in causing aggression is well established, but their action may be influenced by alcohol (Peter Eriksson, *National Public Health Institute, Helsinki, Finland*). Testosterone is also thought to be involved in sexual fantasy and sexual motivation, and trials using testosterone antagonists to treat men with severe paedophilic tendencies are showing some success (Justine Schober, *Harriot Medical Centre, Erie, USA*; Serge Stoleru, *Université Pierre et Marie Curie, Paris, France*). Other modulatory molecules are also involved in the regulation of sexual behaviour. For instance, ejaculation in rats is modified by activation of a certain type of 5HT receptor (Olivier), and oxytocin may be responsible for the calm state following sexual intercourse (Neumann).

The importance of good mother-infant bonding for the development of an infant's brain and its subsequent behaviour is becoming increasingly appreciated. This early experience depends in part on oxytocin, vasopressin and prolactin, the hormone that regulates lactation. The anti-anxiety effects of oxytocin and prolactin support maternal behaviour in rodents and sheep, and in rats, oxytocin promotes protective maternal aggression (Neumann). Small differences in the vasopressin gene seem to correlate with both inter-specific and individual differences in pair bonding and parental care in vole species (Young).

In primates, however, the evolution of the brain indicates that both social and maternal bonding is less dependent on hormones, particularly those stimulated by olfactory cues; instead intelligent strategies based in the greatly enlarged frontal cortex have taken over (Barry Keverne, *University of Cambridge, UK*). Underpinning primate maternal behaviour seems to be the endogenous opioid system that provides an animal with its own internal reward.

A key regulator of stress is the corticosteroid hormone produced by the adrenal glands. As well as its metabolic effects on the body, it acts in the limbic system, where the onset of the stress response and its resolution are mediated by different sets of receptors. This balance may be lost in chronically stressed animals, where changes in structure and function are seen in the limbic system (Ronald De Kloet, *University of Leiden, The Netherlands*).

Because all these interactions are complex and subtle, they can easily be disturbed. A combination of genetic background and early experience make animals more vulnerable to the corticosteroid stress response (Kloet) and the opioid reward system may be distorted by poor mother–infant bonding (Keverne). In monkeys, offspring that are abused by their mothers have lower levels of a 5HT breakdown product than well-treated offspring. This effect may be transferred between generations as levels are lower in abused daughters of mothers who were themselves abused than in those whose mothers had not been abused (Dario Maestripieri, *University of Chicago, USA*). Disturbances in "social" hormones may also contribute to the development of autistic spectrum disorders (Pfaff), and some people with autism have reduced levels of oxytocin and vasopressin (Young).

Ground-breaking work is opening up a further dimension in the understanding of the implications of being a social animal, even to the extent that emotions influence moral decisions (Marc Hauser, *Harvard University, Cambridge, USA*).

La Fondation Ipsen

Established in 1983 under the aegis of the *Fondation de France*, the mission of *La Fondation Ipsen* is to contribute to the development and dissemination of scientific knowledge. The long-standing action of *La Fondation Ipsen* is aimed at furthering the interaction between researchers and clinical practitioners, which is indispensable due to the extreme specialisation of these professions. The ambition of *La Fondation Ipsen* is not to offer definitive knowledge, but to initiate a reflection about the major scientific issues of the forthcoming years. It has developed an important international network of scientific experts who meet regularly at meetings known as *Colloques Médecine et Recherche*, dedicated to six main themes: Alzheimer's disease, neurosciences, longevity, endocrinology, the vascular tree and cancer. In 2007, *La Fondation Ipsen* started three new series of meetings in partnership with: on the one hand the Salk Institute and Nature magazine focused on Biological Complexity, on the second hand with Nature magazine on Emergence and Convergence, the last series being with Cell magazine and the Massachusetts General Hospital titled Exciting Biologies. Since its beginning, *La Fondation Ipsen* has organised more than 90 international conferences, published 65 volumes with renowned publishers and 193 issues of *Alzheimer Actualités*. It has also awarded dozens of prizes and grants.

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