Worldview of Psychiatry

CINP 2004 Congress Preview

The Collegium Internationale Neuropsychopharmacologicum (CINP), the oldest international group dedicated to the advancement of psychopharmacology, will hold its 24th Congress from June 20–24, 2004, in Paris, France.

In this column, we provide program highlights. The Congress will emphasize materials relevant to the concerns of both clinicians who treat patients and basic research scientists who have an interest in neuropsychopharmacology. All major psychiatric disorders, neurotransmitters, receptors, and relevant areas such as clinical treatment and clinical trials, side effect management, biological markers, genetics, and brain imaging will be covered. There will be particular emphasis on new treatments for mental illness and understanding the mechanism of action of psychotropic drugs.

We urge you to attend. Information is readily available at http://cinp2004.com/.

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Neural Substrates of Reward-Related Processes: Implications for Neuropsychiatric Disorders and Development

Monique Ernst, M.D., Ph.D., Chair, and Trevor Robbins, Ph.D., Co-Chair

This symposium will provide unique insights into the neural control of reward-related processes, which form the basis of all motivated behaviors. Our goal is to foster a dialogue between basic neuroscientists and clinical investigators to shed light on the mechanisms underlying motivated actions in health and disease.

Deficits in reward-related processes, which underlie decision-making and motivated actions, are central to any maladaptive behaviors that characterize psychiatric disorders, ranging from depression and antisocial behavior to drug addiction and attention-deficit/hyperactivity disorder. Motivated actions comprise a number of elemental processes, including assessment of situations (or cues), choice of the course of action driven by the attribution of a motivational value to the stimuli, execution of this course of action, anticipation of the outcome, and response to the receipt of the outcome (feedback or reinforcement). These elemental processes are subserved by distinct, albeit overlapping, neural circuits, probably including limbic, prefrontal, and striatal components, which can be affected in overlapping ways, as well as differentially, in distinct neuropsychiatric disorders.

The evidence for these conclusions came initially from basic studies in experimental animals. For example, animal studies have defined neural substrates of reward and motivation within the nucleus accumbens (or ventral striatum) that are modulated by inputs from limbic structures such as the amygdala. Much of these data depended on evidence that rewarded behaviors, such as drug self-administration, were mediated by dopamine-dependent functions of the nucleus accumbens. These dopamine-dependent functions were also shown to be often powerfully controlled by conditioned cues (e.g., conditioned reinforcers) associated with the drug via learning mechanisms sited within limbic structures such as the amygdala.

These findings were followed by studies of humans, for example, with damage to the orbitofrontal cortex and amygdala. Paradigms challenging higher-order decision-making processes and neuroimaging methods using positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) have been used to determine which brain regions are activated in complex decision-making scenarios, including gambling, that involve choice between alternatives with different outcomes. The latter findings have often provided striking converging evidence of the importance of similar prefrontal-limbic-striatal circuitry identified in studies of experimental animals. The human studies have also made it clear that these reward-related processes are influenced by both internal (e.g., mood state, impulsive temperament, arousal, stress) and external factors (e.g., experimental or real life decision-making situations, constraints of economic theory).

Within this framework, in the first part of the symposium, the presenters will provide recent updates of the latest evidence implicating the prefrontal-limbic-striatal systems in reward and decision-making processes. They

will also identify component processes and demonstrate how these processes can be subject to neurochemical modulation.

- Paul Apicella, M.D., Ph.D., will describe how reinforcement and motivation are translated at the cellular level in the ventral striatum (including the nucleus accumbens), using single neuron recordings in nonhuman primates, and will present hypotheses of the differential modulation of dopaminergic, cholinergic, and GABA-ergic neurons in response to appetitive and aversive stimuli.

- Trevor Robbins, Ph.D., will discuss the role and interaction of critical amygdaloid and orbitofrontal components of the reward system for the modulation of mechanisms controlling decision-making and impulsivity in lesion studies of rats. Of note, these processes probably depend on a neural network including these structures interacting functionally with the nucleus accumbens. Dr. Robbins will also describe data indicating interactive but distinct modulatory roles for the monoamine neurotransmitters dopamine and serotonin. Finally, he will highlight the implications of these findings for psychopathology in humans by summarizing findings from experiments carried out in patients with discrete lesions of the frontal lobe, including the ventrolateral prefrontal and orbitofrontal cortex, depression, mania, drug abuse, and other neuropsychiatric disorders.

In the second part of the symposium, presenters will further extend findings from basic neuroscience, such as those presented in the first part, to the understanding of the mechanisms of abnormal motivated behaviors in human psychopathology, including substance abuse disorder, depression, and attention-deficit/hyperactivity disorder (ADHD). They will also provide some preliminary insights into how different trajectories of maturation of key limbic structures can affect behavioral and cognitive development.

- Antoine Bechara, Ph.D., will describe characteristics of the deficits in reward-related behaviors presented by individuals with substance abuse disorders and contrast these deficits with those presented by individuals with discrete brain lesions. He will present data relevant to the hypothesis that the prefrontal cortex normally controls behavior mediated by the interaction of the amygdala with the ventral striatum. In addition, he will show evidence suggesting a dissociation of the function of dopamine and serotonin in the control of habitual and volitional behavior.

- Ian Goodyer, M.D., will introduce the notion of a relationship between normal brain maturation and vulnerability for affective disorders. He will report measures of affective, cognitive, and hormonal systems collected in children that predict later depression, suggesting that major depression requires a mature reward system to be expressed.

- Monique Ernst, M.D., Ph.D., will conclude the symposium by showing task performance and functional neuroimaging data from studies of reward-related behavior in children and adults with and without ADHD. The developmental perspective (healthy children vs. healthy adults) suggests that the well-described propensity for risk-taking behavior of adolescents may be related to different rates of maturation of key structures of the reward system, i.e., the amygdala and nucleus accumbens, and that ADHD may be, in part, secondary to a prolonged immaturity of these structures.

The recurrent theme spanning these 5 presentations involves the role of the ventral striatum, amygdala, and orbitofrontal cortex in reward-related processes, their modulation by monoamines, and their differential contribution to various diatheses. Another theme will show how simple elements of behavior may provide the building blocks of much more complex decision-making processes that exemplify the highest levels of cognitive function and how this integration may depend on complex loop circuitry between cortical and subcortical structures. Finally, it will be shown how disorders marked by abnormal impulsivity or abnormal inhibition can be explained by reference to deficits in reward-related behaviors, the neural substrates of which have been established from work in experimental animals. Ultimately, a better understanding of the biological and environmental mechanisms underlying psychopathology, particularly in a developmental context, will enable the development of novel strategies for prevention and treatment of psychiatric disorder.