

Cognition: The Ultimate Brain Function

Neuropsychopharmacology Reviews (2011) 36, 1–2; doi:10.1038/npp.2010.171

This fourth issue of *Neuropsychopharmacology Reviews* focuses on cognition, the ultimate function of the brain. Arguably, most, if not all, of the major neuropsychiatric disorders such as schizophrenia, depression, and anxiety are cognitive in nature. Increasingly, it is realized that symptoms such as delusions and hallucinations, as well as other motivational and emotional signs, may have important cognitive elements. These arise, for example, from aberrant learning and associative factors, impaired attributional systems, and deficient control processes that are recruited to regulate emotional outputs and inappropriate behavioral responses. In general, cognition refers to those, sometimes mysterious, covert processes that have to be inferred from behavior. Cognitive processes include seemingly miraculous products of modular processing to produce, for example, representational knowledge such as language, and mechanisms that intervene between stimulus and response, often in a ‘top-down’ or ‘executive’ manner to mediate and resolve competition between what are often autonomous neuro-cognitive systems. Deficits in such cognitive processes as working memory are now acknowledged to be important factors in their own right that determine the likelihood of rehabilitation in disorders such as schizophrenia, and this has led to recent initiatives of the National Institute of Health such as the MATRICS project on the measurement and remediation of cognitive functions for the purpose of clinical trials (Green, 2007). Moreover, the state of psychiatric genetics is helping us to realize that the accurate definition of phenotype, and the corollary identification of cognitive endophenotypes, is a vital aim in any program that seeks to understand the genetic basis of psychopathology.

Great advances in cognitive neuroscience over the past two decades, aided by technological innovations in several modalities of brain imaging, as well as increased sophistication in computational theory and cognitive psychology, have inspired psychopharmacologists and biological psychiatrists alike to characterize the properties of candidate cognition-modifying compounds, beneficial or otherwise. In this Special Issue, we have tried to capture some of the excitement of this burgeoning area of research, and how it may inspire future advances in the field, with an emphasis on translational strategies.

We have focused on current hot-spots of debate and potential growth areas by commissioning well-refereed reviews (often entailing novel collaborations) that either complement one another or stand apart, like beacons, to

inspire new discovery. We have chosen not to re-review areas where recent authoritative pieces have removed the need (eg, the role of noradrenergic mechanisms (eg, Arnsten, 2009)).

The result is a collection of 16 substantial reviews sequenced to highlight their most obvious inter-relationships. The series begins with a review by Coull *et al* that uniquely synthesizes neuropsychopharmacological and neuroimaging evidence from human and animal studies on timing—a fundamental and yet intangible process that permeates and underlies most cognitive functions. Kenemans and Kähkönen help us to appreciate the potential of contemporary methods in human electrophysiology, including magnetoencephalography, which have the necessary precision and temporal resolution to illuminate attentional and response preparatory processes and how they are altered by psychoactive drugs. Many such effects arise from drugs affecting monoaminergic systems and so we have covered the important advances accruing from analyses of the monoaminergic and cholinergic systems. Thus, Hasslemo and Sarter review progress in understanding the role of cholinergic systems in attentional and memory processes at a mechanistic level. Several articles then converge on the implications of remarkable advances in understanding the roles and modes of the central dopamine projections that may inspire the resolution of similar questions about the role of the 5-HT systems. Articles by Boureau and Dayan, and Cools *et al* both illustrate the advantages of combining new approaches in computational and imaging neuroscience to gain fresh and complementary perspectives on such classical issues of putative unitary functions and opponency of these monoaminergic systems. Rogers shows how such analyses may inform our understanding of decision-making processes in humans and Frank and Fossella introduce a pharmacogenetic perspective, again with emphasis on monoaminergic systems.

Possible clinical applications of advances in understanding of cortico-limbic circuitry under neuromodulatory control are then covered by two contrasting chapters on cognition in depression. One (by Elliott *et al*) covers the implications of new discoveries about reward systems and emotional regulation and the other (by Pizzagalli) identifies, through meta-analysis, a possible neuroendophenotype for treatment of depression based on hyperactivity of the rostral anterior cingulate cortex, which is then interpreted in the context of other elements of this circuitry and their purported cognitive functions.

The next article (by Volkow *et al*) provides perhaps the best evidence relating to possible cognitive enhancement, mainly through stimulant medications in the treatment of attention-deficit hyperactivity disorder (ADHD). The great interest in cognitive enhancing drugs, relevant, for example, to programs in schizophrenia, is then reviewed from the perspective of animal studies of memory and executive function (by Floresco and Jentsch) before Hardt and Nadel provide a stimulating and timely update on theoretical advances in understanding memory systems, especially for episodic memory.

The last decade has seen enormous advances in revealing how glutamatergic processes affect plasticity and learning and this is represented here by a survey of the fascinating processes underlying extinction, their susceptibility to manipulation through glutamatergic drugs and the novel implications for clinical treatment of such conditions as anxiety and addiction (by Myers *et al*). Corlett *et al* illustrate another side of the NMDA receptor coin: the imaginative use of the ketamine model of psychosis in humans to understand the cognitive and neural basis of delusional phenomena. Lesh *et al* then review the characterization of cognitive deficits in schizophrenia from a particular theoretical position that emphasizes impairments in cognitive control processes.

We look forward to the next issue of *Neuropsychopharmacology Reviews* with its clinical and applied themes,

by reviewing a vital element of clinical trials—the neuro-cognitive basis of the placebo effect (by Benedetti *et al*).

Last, but by no means least, these substantial reviews are highlighted by an extraordinarily stimulating set of ‘hot topics’, which help to fill in the gaps of our inevitably incomplete coverage (and definitely enable us to say we have considered both ‘hot’ and ‘cold’ cognition!).

It has been a privilege to edit this Special Issue and I would like to pay tribute to the efforts of the authors, referees, as well as my co-editing colleagues Peter Kalivas, Gwenn Smith, Kathryn Cunningham, and Diane Drexler.

DISCLOSURE

TWR discloses his consultancy for Cambridge Cognition, Pfizer, E Lilly, Lundbeck, GlaxoSmithKline, and Allon Therapeutics, as well as recent research grants from Pfizer, E Lilly and GlaxoSmithKline.

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