Cognitive Systems: Workshop Proceedings

October 23-25, 2011
Rockville, MD

Background

The Research Domain Criteria (RDoC) project is designed to implement Strategy 1.4 of the NIMH Strategic Plan: *Develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures.* NIMH intends RDoC to serve as a research framework encouraging new approaches to research on mental disorders, in which fundamental dimensions that cut across traditional disorder categories are used as the basis for grouping patients in clinical studies. RDoC represents an inherently translational approach, considering psychopathology in terms of dysregulation and dysfunction in fundamental aspects of behavior as established through basic neuroscience and behavioral science research. The major RDoC framework consists of a matrix where the rows represent specified functional *Constructs*, concepts summarizing data about a specified functional dimension of behavior, that are characterized in aggregate by the genes, molecules, circuits, etc., responsible for it. Constructs are in turn grouped into higher-level *Domains* of functioning, reflecting contemporary knowledge about major systems of cognition, motivation, and social behavior. In its present form, there are five Domains in the RDoC matrix: Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Systems for Social Processes, and Arousal/Regulatory Systems. The matrix columns specify Units of Analysis used to study the Constructs, and include genes, molecules, cells, circuits, physiology (e.g., heart-rate or event-related potentials), behavior, and self-reports. The matrix also has a separate column to specify well-validated paradigms used in studying each Construct.

The RDoC matrix is being developed to serve as a heuristic, and it is subject to change with scientific advances from the field. To "build the matrix," NIMH has been bringing together leading experts to coalesce and articulate the state of knowledge for each of the five domains in six meetings. Six meetings are planned: this workshop, focused on the Cognitive Systems Domain, was the fourth in the series.

For detailed information about RDoC, proceedings from prior workshops, and the updated matrix, please refer to the RDoC web page.

Workshop Proceedings

This workshop on the Cognitive Systems Domain was convened to reach agreement on those Constructs most likely to comprise this Domain and advance research linking psychopathology with integrative neuroscience. Other critical goals of the workshop included: (1) clarifying formal definitions of the Constructs agreed to be included within this Domain; (2) clarifying what is known about the Units of Analysis for each of the Constructs; and (3) compiling questions that remain unanswered, and outlining potential avenues of research that will answer these questions.

The end product of this workshop was a set of Constructs in the Cognitive Systems Domain along with an agreed-upon definition for each, incorporating how the field views each Construct and how best to clarify the distinctions among cognitive constructs that overlap. For instance, working memory plays a role in sustained attention, and cognitive control relies to a certain extent on working memory. The workshop also provided an annotated listing (based on current knowledge) of the elements populating the RDoC matrix with respect to the genes, molecules, cells, circuits, physiology, behavior and self-reports comprising each Cognitive Systems Construct, as well as identifying promising and reliable behavioral tasks that can be used to assess function within a Construct. The entries in the various Units of Analysis may be considered as priority elements for describing research participants in clinical research grant applications. In the RDoC matrix, the different units of analysis may serve as independent or dependent variables, depending on the purposes and goals of the research.

The NIMH RDoC working group initially proposed the following Constructs for consideration: Attention, Perception, Declarative Memory, Language Behavior, and Cognitive (Effortful) Control. Workshop members were invited to evaluate, modify, and define the Constructs, or to consider new Constructs if warranted.

Based on each individual's scientific expertise, the workshop participants were assigned to one of three "Construct groups." For purposes of efficiency, the Constructs of Attention and Perception were jointly considered, as were the Constructs Declarative Memory and Language; the third group of participants considered Cognitive Control. The Attention and Perception group was moderated by Judith Ford, the Declarative Memory and Language group by Dwight Dickinson, and the Cognitive Control group by Ed Smith. The full list of members for each group is provided below.

Preliminary Discussion

Initial efforts were directed at the Constructs proposed for consideration: Attention, Perception, Declarative Memory, Language, and Cognitive Control (with Working Memory acknowledged as considered at an earlier meeting as described previously). There was broad agreement that these Constructs were an excellent starting point and that there was no need to modify them or to add additional constructs at this point. Nonetheless, it was decided that the potential for modification or addition would be revisited if discussion from breakout groups suggested the need for such consideration. As is the case for all RDoC Domains/Constructs, additions or modifications may be made based on new data as the process develops.

The first task for the three breakout groups was to develop the definitions for the Constructs and then report back to the entire group for peer review and refinement. This process also included the elaboration of the definitions in terms of the integrated systems that compose the critical processes involved with each construct. Further clarification was provided during efforts to articulate how each Construct is distinct from, and overlaps, other relevant constructs or related processes. Following several iterations of breakout groups working toward these goals and reporting their efforts to the larger group and integrating feedback, consensus definitions were achieved. Later, workgroups worked to "populate" the Units of Analyses of the RDoC matrix with the best available empirical evidence.

The definitions of the Constructs are provided below, followed by a summary of the workshop discussion.

Construct Definitions

1. **Attention:** Attention refers to a range of processes that regulate access to capacity-limited systems, such as awareness, higher perceptual processes, and motor action. The concepts of capacity limitation and competition are inherent to the concepts of selective and divided attention.

2. **Perception**: Perception refers to the process(es) that perform computations on sensory data to construct and transform representations of the external environment, acquire information from, and make predictions about, the external world, and guide action.

3. **Declarative Memory:** Declarative memory is the acquisition or encoding, storage and consolidation, and retrieval of representations of facts and events. Declarative memory provides the critical substrate for relational representations—i.e., for spatial, temporal, and other contextual relations among items, contributing to representations of events (episodic memory) and the integration and organization of factual knowledge (semantic memory). These representations facilitate the inferential and flexible extraction of new information from these relationships.

4. **Language:** Language is a system of shared symbolic representations of the world, the self and abstract concepts that supports thought and communication.

5. **Cognitive Control:** A system that modulates the operation of other cognitive and emotional systems, in the service of goal-directed behavior, when prepotent modes of responding are not adequate to meet the demands of the current context. Additionally, control processes are engaged in the case of novel contexts, where appropriate responses need to be selected from among competing alternatives.

6. **Working Memory:** See Working Memory: Workshop Proceedings (July 11-13, 2010) at: http://www.nimh.nih.gov/research-funding/rdoc/working-memory-workshop-proceedings.shtml

Summary of Construct Group Deliberations

Attention and Perception Group

Attention

Definition: Attention refers to a range of processes that regulate access to capacity-limited systems, such as awareness, higher perceptual processes, and motor action. The concepts of capacity limitation and competition are inherent to the concepts of selective and divided attention.

Elaboration of Cognitive and Neural Systems

Two sets of processes are critical to the construct of attention. First, many brain systems (perceptual, cognitive, motivational, emotional) compete for control of attention. The output of this competition is a pattern of distributed modulation that seeks to increase the priority of some sources of information, while decreasing the priority of others, a process called the *control of attention*. Second, these changes in priority lead to modulations of local circuit interactions within target regions that produce the enhancement of some sources of information and suppression of others, called the *implementation of selection* (Luck & Gold, 2008). Attentional deficits can arise either because of failures of *attentional control* or *attentional implementation***.** Within all attentional pathways, therefore, care should be taken in differentiating processes related to disorders of control from those related to disorders of implementation.

Many different systems influence the control of attention, including: motivational inputs, such as those arising from the hypothalamus/limbic system (e.g. hunger, sexual drives); salient sensory inputs; reward systems; and emotion systems. It was noted that arousal has important effects on attention; however the construct of arousal is primarily represented in the Arousal/Modulatory Systems domain.

Saliency

The term saliency is often used to describe the degree to which a given perceptual input competes for attentional control. Much perceptual activity occurs with low saliency and so does not compete effectively for attentional resources until acted upon by attentional systems (Desimone & Duncan, 1995). However, some outputs of the perceptual system may be sufficiently salient to compete effectively for attention on their own. Examples of inherently salient stimuli include aversive or intense sensory stimulation in all modalities, motion or temporal change within the visual system, or deviations from regularity within the auditory system. These may be thought of as dedicated bottom-up attentional control subsystems that have evolved to permit attention to be adaptively deployed.

Bottom Up/Top Down Processes

Top-down information influences the allocation of attention by means of representations of goals and relevance, which then interact with incoming information to prioritize sources of information that match the goals. These top-down influences on priority are merged with bottom-up priority signals, to determine the actual allocation of attention at any given time.

Although these definitions of top-down and bottom-up influences have been well studied, and much has been clarified in the cognitive literature, they become more complex when applied to goal-directed behavior (organized in the visceral nervous system including subcortical and limbic structures), influencing attentional allocation in the somatic nervous system (including association cortex and primary and secondary cortices). An alternative to the top-down and bottom-up distinction of attention control from the classical neurophysiology literature is an external (somatic sensorimotor neocortex) to internal (visceral limbic) control dimension within each hemisphere. On this dimension, cognitive representation in association cortex is in the middle, between visceral and somatic constraints.

Although all parts of the brain are potentially influenced by attention, the effects of attention tend to be more pronounced on hierarchically higher brain regions in which processing is more complex and the availability of resources more limited (Kastner et al., 1998). Thus, within both the auditory and visual systems, attentional influences are greater on later stages of processing than on earlier stages of processing.

Circuits: Transmission of Information Through Sensory Systems

Attention may influence the feed-forward transmission of information through sensory systems, as well as local circuit processing within specific brain regions (Hillyard et al., 1998; Reynolds et al., 1999). Multiple competing networks mediate attentional control depending upon specific task demands. Two major attentional networks have been identified, the dorsal and ventral, which involve interactions between frontal and parietal cortex and subcortical structures (Corbetta & Shulman, 2002). In the psychological literature, attention is categorized according to multiple schemata, such as spatial vs. object; featural vs. temporal; divided vs. selective; alternating vs. sustained; single channel vs. multichannel; unimodal vs. crossmodal; exogenous vs. endogenous; overt vs. covert; internal vs. external. How these psychological divisions map onto underlying neural circuits remains an area of active research.

Clarifying Vigilance and Sustained Attention

The term vigilance is currently used in two discrete contexts. The first is sustained attention, which is largely equivalent to goal maintenance and is subsumed under the construct of cognitive control within RDoC. The second refers to appropriate or inappropriate sensitivity to specific classes of information, with particular involvement of limbic/amygdalar systems. This second definition applies to clinical populations where individuals can show sustained hyper- or hypo-vigilance (Ohman et al., 2001), and is included as one aspect of the construct of attention as discussed in this section. Although a clear consensus in the field has not been reached, workshop participants propose the term *sustained attention* for the former usage, and the term *vigilance* for the latter. Note that the second definition of attention is shared with the "Responses to Potential Harm" construct in the Negative Valence Domain, which is seen as generating the motivational aspects of vigilance.

The concept of differential processing is inherent in the concept of attention (i.e. the same object is processed differently when attended vs. unattended). Thus, in discussing attention it is critical to define the *neutral* state that represents the unattended condition. Many controversies regarding the operation of attention are, in fact, controversies of what should be considered the neutral state. Although many definitions can be used (e.g., sleep vs. wake), in most circumstances a state corresponding to operation of the *default mode* (i.e., awake but with resources devoted primarily to internally driven representations) might be most appropriate. In cognitive control paradigms, differentiation between attended and unattended state will depend upon specific task instructions.

Relations and Distinctions with Other Domains/Constructs

Recognizing that the Domains and Constructs naturally overlap, it seems useful to clarify how each Construct might be differentiated from other Constructs or the processes that often play integral roles.

Attention can be differentiated from perception by the degree of external stimulation involved. Attention, if sufficiently strong, can lead to illusions and misperceptions, but percepts driven entirely by attention are, under normal circumstances, weak compared to those driven by sensory inputs. Perception may compete successfully for capture of attentional control pathways. In such cases, an attentional capture signal may be viewed as the output of the perceptual systems.

Attention and Cognitive Control

Attention may be differentiated from cognitive control based upon the degree of competing information that is inherent to the task. It was acknowledged and agreed upon among the broader workshop members that cognitive control most often requires attentional processes, and thus cognitive control tasks also test attention. However, for purposes of this stage of the RDoC initiative, it was considered most appropriate to classify executive attention under the Cognitive Control Construct.

Valence and Arousal

Attention is interdependent with valence and arousal systems. Valence and arousal systems exert strong control on attention, and attention regulates perceptual input into valence and arousal systems. Nevertheless, it is worthwhile to view attention as a separate process by which these systems modulate both each other and other aspects of cognition.

Other Issues

Although attention interacts with all other cognitive systems, it is critical not to attribute failures elsewhere in the system to failures in attention. Attentional deficits should be inferred only when direct manipulations of attention (e.g., manipulations of attentional load, direction of attention, or assessments of capacity) are employed. Moreover, specific attentional subsystems (e.g., spatial vs. object, focused vs. divided, dorsal vs. ventral systems) should be specified whenever possible. Although exact brain systems subserving attention remain under investigation, it is anticipated that attention networks may correspond closely to resting state networks, as illustrated by Yeo and colleagues (2011).

Perception

Definition: Perception refers to the process(es) that perform computations on sensory data to construct and transform representations of the external environment, acquire information from and make predictions about the external world, and guide action.

Elaboration of Integrative Systems

Perception reflects an interplay between 1) bottom-up, sensory-driven processes, 2) top-down modulatory influences (from cognitive control, attention, memory, limbic/motivational systems, etc.), and 3) lateral interactions among and within sensory regions. Some aspects of perception are driven by the *feed-forward* sweep of sensory information and occur with relatively limited input from higher brain regions. The role of top-down modulatory influences increases anatomically and temporally with later stages of processing and with iterative, re-entrant connections. In addition, perception of sensations is affected by actions that produce those sensations, through the action of *corollary discharge* and *efference copy* mechanisms in an action-perception loop.

Bottom Up/Top Down Processes

In general, perception reflects processes that localize to well-described unimodal and multimodal sensory regions of the brain. Bottom-up inputs arise from sense organs (e.g., retina) that project via well-known pathways to cortex (e.g., via cranial nerves, lateral/medial geniculate nuclei), which, in turn, send (glutamatergic) feed-forward inputs primarily into granular layers of primary and secondary sensory cortex. Top-down influences can occur either through cortico-cortical connections, which originate via (glutamatergic) feed-back patterns of input primarily into supra-/infra-granular layers of cortex, or via modulatory systems (catecholamines, acetylcholine, peptides, etc.) which may innervate across multiple cortical layers. Within each cortical region, horizontal excitatory (glutamatergic) connections between pyramidal cells, and local inhibitory (GABAergic) interactions modulate the timing, salience, and organization of the processing of sensory primitives (e.g., visual features) and sculpt local input/output relationships. Interaction among inputs from different sensory modalities (auditory, visual, somatosensory) can occur early in processing, leading to multisensory influences on perception.

Functional Components

Perception can occur in the service of either 1) action or 2) identification, with these processes occurring potentially in parallel and location information being integral to both. Not all perception involved in control of action reaches conscious awareness. Similarly, action can commence before identification processes are complete.

Circuits: Neural Pathways

In the visual system, two distinct pathways subserve perception for action (dorsal system, “where” or “how” pathway) vs. perception for identification (ventral system, “what” pathway). The dorsal and ventral systems receive preferential input from the subcortical magnocellular and parvocellular feed-forward pathways, respectively. These systems originate in the retina and are segregated at the level of the lateral geniculate nucleus and primary sensory cortex. Because of the differential response properties of these subcortical pathways, the dorsal and ventral stream pathways have access to overlapping but differential sensory information (e.g., motion and response to low luminance/low contrast information is represented primarily in the magnocellular pathway; high spatial frequency and color information in the parvocellular pathway). However, there is substantial interaction between the dorsal and ventral streams (Sehatpour et al., 2010).

Transmission of information is much more rapid within the magnocellular/dorsal stream pathway than the parvocellular/ventral stream pathway. Thus, information transmitted through the dorsal pathway precedes information transmitted through the ventral pathway and may frame perception in the ventral stream pathway by activation of low-resolution representations that are then filled by higher resolution information reaching ventral stream via the parvocellular pathway. Dorsal stream information may reach prefrontal brain regions rapidly (e.g., <100 ms) following sensory input, and it interacts with frontal, cognitive control systems and medial temporal declarative memory systems to influence perception for identification within the ventral stream pathway. In considering disorders of perception, care should be taken in specifying neural pathways and interactions involved in the computation within a framework of perception for action or perception for identification.

Within the auditory (and somatosensory) pathways, separate dorsal/ventral pathways with preferential roles in action versus identification have also been identified but are less well described and more controversial than in the visual system. Notably, however, both systems receive inputs from the same subcortical pathways, so that temporal distinctions in processing may not occur to the degree that is inherent within the visual system.

Processing of stimulus features occurs in parallel within multiple cortical subregions. The concept of hierarchical processing is inherent within the concept of perception. Lateral interactions may occur both within and across sensory subregions. Interactions may occur between subregions at similar levels of the processing hierarchy, or by feedback from hierarchically higher regions to prior processing stages. A challenge for perceptual systems is to extract meaningful information (which could be defined as information that can be used to guide goal-directed activity), such as features, objects, contrasts, change, or categorization, from the overwhelming amount of levels of sensory information that impinges constantly upon the sense organs. Thus, perceptual systems do not provide bitmap-like representations of the external environment, but rather highly processed representations, to which other cognitive systems may gain access. The types of information extracted from the environment are highly dependent upon prior experience and individual competencies and may differ across individuals. Different aspects of the external environment are represented simultaneously within different regions of cortex devoted to perception.

Relations and Distinctions with Other Systems

More on Overlap: Bidirectional Influences or Processes

A challenge for other cognitive systems, such as cognitive control or valence systems, is to gain access to the correct level of perceptual information to solve the task at hand. For instance, attentional systems act on perceptual systems in the service of perceptual selection.

Some aspects of perceptual processing are generally considered to occur prior to the allocation of attention (i.e., preattentive), whereas others are resource intensive. Attentional and arousal systems regulate the degree of resources devoted to perceptual processing, ideally in the service of optimizing resource allocation. These systems include entrainment systems, which subserve temporal allocation of processing resources based upon underlying rhythmicity of inputs and actions.

In addition to providing inputs that guide behavior, perception is itself heavily guided by behavior. Especially in the visual system, perception is heavily influenced by motor rhythmicity (active sensing), which influences timing and location of fixations. Although the majority of perceptual information is relayed through sensory cortex, direct sensory inputs to the amygdala or other limbic regions may bypass cortex (particularly in the visual system), permitting rapid input of relatively primitive sensory information into positive and negative valence systems, even in the absence of conscious awareness.

Some of these issues may be resolved by studies that clarify the temporal organization of perceptual processes. For instance, temporally organized activity within perceptual systems may be assessed using event-related potentials (ERPs), while spatially organized activity is better represented using functional magnetic resonance imaging (fMRI). These techniques can be used to examine the interplay between bottom-up, top-down (e.g., cognitive control), and motivational (e.g., positive/negative valence system) influences. Multiple paradigms are available that permit fine-grained analysis of integrity of perceptual processing systems across disorders (see Paradigm section of the Matrix). In addition, the speed of different perceptual processes can be assessed using behavioral paradigms, such as backward masking, in which labile representations can be disrupted at varying intervals following stimulus presentation.

Control Processes Interacting with Perception

Perceptual systems typically serve to limit the influence of repetitive stimuli through processes such as habituation or desensitization. Such processes may act at multiple levels, from the sense organs to cortex. *Gating* refers to the relative decrease in response strength to the second stimulus in a sequence compared to the response to a prior stimulus. In some cases, closely spaced stimuli may also lead to increased response, termed facilitation. Excitation and facilitation can also occur with simultaneously presented stimuli, depending on factors such as similarity, proximity, and spatial arrangement.

Many aspects of perception improve with practice, a phenomenon known as *perceptual learning* (PL). Although we are not yet at a point where a single, comprehensive model of PL can be fully specified, recent work suggests that PL involves two mechanisms: external noise exclusion and stimulus enhancement. However, not all PL is perceptual: PL has also been hypothesized to involve activity in a decision or response unit in which the reweighting of specific representations during decision processes occurs. Therefore, while abnormalities in perceptual learning have been demonstrated in psychopathology, it is important to isolate to the extent possible perceptual from higher-level cognitive processes involved in PL.

Perception and Attention

Perception interacts closely with attention and, to a certain extent, depends on it. Although perception usually requires some degree of prior attention allocation (reductionistically, little perception occurs in coma), the degree of attention required is usually not large. Care should be taken not to attribute deficits in perception to deficits in attention, without direct manipulation of attentional function.

Cognitive control systems affect perception primarily through control of attention. Perception affects cognitive control through determination of information reaching cognitive control pathways, and through perception of information needed to perform cognitive control tasks. Since perception is not a unitary phenomenon but occurs in parallel along "perception for action" (e.g., dorsal) and "perception for identification" (e.g., ventral) pathways, it is useful to consider both types. Perceptual information may be encoded in a form that remains accessible over time to other cognitive systems, such as working memory, cognitive control, and declarative memory systems. This may be seen as the last stage in processing within the perceptual system related to working memory or other systems, or the first stage of processing within the upstream systems. For the purposes of RDoC, encoding of information (for working memory, cognitive control, and so on) is treated as a property of the perceptual systems.

Cognitive systems relevant to other domains (e.g., negative valence, positive valence, or arousal systems) affect perception primarily though attention. Perception affects these systems by controlling information input via both "perception for action" and "perception for identification" systems.

Declarative Memory and Language Group

Declarative Memory

Definition: Declarative memory is the acquisition or encoding, storage, consolidation, and retrieval of representations of facts and events. Declarative memory provides the critical substrate for relational representations—i.e., for spatial, temporal and other contextual relations among items, contributing to representations of events (episodic memory) and the integration and organization of factual knowledge (semantic memory). These representations facilitate the inferential and flexible extraction of new information from these relationships.

Elaboration of Integrative Systems

Declarative memory is mediated by multiple brain networks. It is most often associated with the hippocampus, its interactions with medial temporal lobe (MTL) cortices, and their interactions with the posterior association cortices involved with, for example, perception, language, and spatial processing. These interactions provide both the input to the MTL and distributed, lasting representations of the resulting memories. Declarative memory processing is modulated by diencephalic and brain stem systems, including oscillatory coordination. There are also essential interactions between the MTL and both frontal lobe and parietal lobe regions involved in attention, cognitive control, and working memory, especially in effortful, cognitively mediated aspects of encoding and retrieval. Declarative memory is also known to interact with habit and procedural systems through MTL, frontal, and striatal connections.

Relations and Distinctions with Other Systems/Domains/Constructs

Declarative memory interacts with emotion, motivation, as well as perceptual processes and other cognitive processes. It is used in service of higher order functions, such as in communication, inferential reasoning, spatial navigation, conscious recollection, and other goal-directed behavior.

Declarative memory provides the record of the outcomes of experience, rather than the tuning and modification of cognitive processors that support procedural or non-declarative memory, including procedural/habit memory, emotional memory, implicit/automatic memory, and representational activation.

Language

Definition: Language is a system of shared symbolic representations of the world, the self, and abstract concepts that supports thought and communication.

Elaboration of Integrative Systems

Language involves a mapping between thought (production) and sensory representations (comprehension) via a symbolic system of multiple representations (which include prosody, phonology, syntax, orthography and lexical-semantics).

Relations and Distinctions with Other Systems

Word, sentence, and discourse comprehension and production involves the activation and retrieval from memory of concepts about objects, facts, events and event schemas, social relationships and links among them. At the level of sentences, language comprehension and production further involve the construction of propositional meaning through combinatorial processes that draw upon hierarchical structural representations (including syntax). In text and discourse, propositions are sequenced and structured across causal, spatial, referential and temporal dimensions to form a coherent representation of overall meaning.

Formulating and understanding language involves the use of pragmatic and real-world knowledge, as well as non-verbal behaviors, allowing for flexible and effective social interaction.

Finally, while the functional capacity for language is highly specialized in humans, it may draw upon mechanisms and neural substrates that mediate cognition and communication in non-human species.

Cognitive Control

Definition: A system that modulates the operation of other cognitive and emotional systems in the service of goal directed behavior when prepotent modes of responding are not adequate to meet the demands of the current context. Additionally, control processes are engaged in the case of novel contexts, where appropriate responses need to be selected from among competing alternatives.

Elaboration of Integrative Systems

Cognitive control involves multiple subcomponent processes, including the ability to select, maintain, and update goal representations and performance monitoring and other forms of adaptive regulation. The implementation of these processes includes mechanisms such as response selection and inhibition or suppression.

Relations and Distinctions with Other Systems

Given that it is essentially a domain-general modulatory system, cognitive control is relevant to the performance of many tasks, such as language and perception. However, cognitive control is distinct from other mechanisms in systems such as language and perception that coordinate and resolve ambiguity and conflict through local interactions.

Working Memory

Cognitive control overlaps with working memory in the specific domain of the updating and maintenance of goal representations. Cognitive control is distinct from working memory in so far as working memory is not restricted to the maintenance of goals.

Executive Attention

Executive attention is a component of cognitive control because both goal selection, and goal updating and representation are central processes in both. Cognitive control is distinct from other forms of attention in so far as attention is more closely associated with input selection. The goal maintenance function of cognitive control is considered to be an essential feature of sustained attention, including sustained selective attention (e.g., Sarter tasks).

Motivation

Cognitive control interacts with aspects of motivation and persistence (see Positive Valence Workshop).

Working Memory

See Working Memory: Workshop Proceedings (July 11-13, 2010).

NIMH encourages comments on any aspect of the workshop and proceedings outlined here. Please send comments to: rdoc@mail.nih.gov.

Cognitive Systems Matrix Specifications

Units of Analysis							
Genes	**Molecules**	**Cells**	**Circuits**	**Physiology**	**Behavior**	**Self-reports**	**Paradigms***
ATTENTION							
Dopamine receptor genes (e.g., D4, D5); DAT1; Serotonin receptor gene	**Implementation:** GABA, glut **Control:** Glut, Serotonin; dopamine; histamine; Ach	Parvalbumin-positive interneurons	**Implementation:** TRN; pulvinar; local circuit interactions **Control:** ascending/descending information pathways; amygdala (vigilance); Atentional systems: dorsal attention network (superior parietal lobe, frontal eye fields, DLPFC); ventral attention network (temporal parietal junction (TPJ), VPFC, insula); basal forebrain limbic system Balance between task positive network (TPN) vs DMN	**fMRI** Sensory areas from peripheral to central. **ERP-- Auditory:** processing negativity; P1, N1, N2; P300; neural oscillations. **Visual**:N2pc; Selection modulations of sensory ERP components; negativity (SN); P300; slow waves; neural oscillations **Peripheral physiology** both modalities: Heart rate deceleration; Pupil dilation;	Spatial attention; Object/feature attention; ANT task Distractibility; Attentional lapses (e.g., RT variability) vs sustained attn; Psychophysics	Yes (but often not attention that is impaired)	dichotic listening, visual search, spatial and non-spatial cuing paradigms, dual task paradigms (attentional blink and psychological refractory period paradigm); inter-modal selective attention; blocked channel-selection tasks; distraction paradigms (capture); time-series of response times to extract variability and frequency domain analyses ***(target detection tasks in the absence of competition are considered measures of sustained attention and not selective or divided attention, which are subsumed under cog control)***

*Many of these paradigms can be adapted for use in behavioral, ERP and fMRI protocols.

Genes	**Molecules**	**Cells**	**Circuits**	**Physiology**	**Behavior**	**Self-reports**	**Paradigms**
PERCEPTION							
Component Process (“subconstruct”): Visual Perception							
Dysbindin / NRG1/ Neuroligin / Neurexin	Glutamate, GABA. NMDA, Serotonin, Ach, Catecholamines, peptides	Magno (non-linear gain control). Parvo. “Frame and fill”. Pyramidal, parvalbumin positive interneurons.	**Subcortical:** magnocellular, parvocellular, koniocellular. **Cortical:** dorsal/ventral streams; cortico-cortical connections into supra- and infra-granular layers.. **Non-retinogeniculate:** Superior colliculus, Suprachiasmatic nucleus. **Local circuitry** implicated in contextual fields and association fields (responsible for	Oscillations (scalp EEG, LFP, and single/multi-unit). ERP components: All of the sensory evoked potentials (from stimulus onset through N1), Ncl, ssVEP, tVEP. BOLD (activation) of cortical regions. Adaptation/habituation.	Stimulus detection. Discrimination, identification and localization. Perceptual priming. Visual acuity. Reading. Perceptual learning.	Perceptual anomalies of schizophrenia and depression.	Scheme I. Stages of Vision. Early vision retinotopic representations, local computations. Intermediate vision Nonlocal properties of images, transformations beyond retinotopic representations (e.g., surface properties of the object independent of light, head position). Late vision Representations of external objects (e.g., object identification, classification, visually guided action). Scheme 2. Commonly Used Research Paradigms Vernier discrimination; Object recognition/perceptual closure /perceptual organization; object perception; contour integration/interpolation; face identification; emotion expression identification;

			the influence of spatial context on target processing): lateral interactions; top-down interactions				Parallel/serial search; Reading; contrast sensitivity; lateral facilitation; biological motion processing; coherent motion; bistability; multistability; figure ground; backward masking; visual illusion susceptibility; cross modality paradigms. Other schemes. Re-entrant processing. Action-Perception loops.

Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-reports	Paradigms
Component Process ("subconstruct"): Auditory Perception							
BDNF	Glutamate/ GABA/ NMDA/ serotonin/ ACh	Cochlear hair cells; Ribbon synapses; cortical and limbic inhibitory interneurons.	Nodes in circuits: Cochlea; brainstem; MGN; A1; STG; ant. Insula; Inferior Colliculus. Circuits: Dorsal/ ventral streams; Corticofugal.	Sensory ERPs (e.g, P50, N1), Auditory steady-state response (ASSR); Intracortical EEG, Mismatch negativity (MMN); P3a; metabolic changes (fMRI, PET); startle and PPI; neural oscillations (e.g., GBR); adaptation /habituation. fMRI: regulation of hemodynamic components of sensory response and habituation.	Stimulus detection. Spatial localization. Perceptual identification. Perceptual priming. Perceptual learning.	Auditory hallucinations; Hyperacusis	Tone matching; deviance detection, regularity and change detection; McGurk (multisensory); auditory scene perception (e.g., streaming); bistability; novelty/oddball detection; detection of speech in noise, cross-modal interactions; auditory masking; Manipulation of ISI; and intensity Object perception; Categorization; Gating; self-monitoring; inhibitory control; same-different tasks; tone detection (e.g., JND tasks) Action-Perception loops.

Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-reports	Paradigms
Component Process ("subconstruct"): Olfactory Somatosensory Multimodal Perception							
							Manipulation of ISI, intensity for somatosensory stimulation; smell identification;

Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-reports	Paradigms
DECLARATIVE MEMORY							
BDNF, KIBRA	Cholinergic, Glutamatergic, Noradrenergic, and other neurotrans	Pyramidal cells, granule cells, many types of inhibitory and	Intriinsic hippocampal circuitry (e.g., DG, CA1, CA3, subiculum); extrinsic hippocampal circuitry	LTP/LTD, NMDA-related synaptic plasticity, AMPA-related synaptic plasticity, place cell activity,	Learning, recall, discrimination, familiarity, recognition	Cognitive Assessment Interview	Paired associate learning; delayed recall; transitive inference; acquired equivalence; list and story learning

	mitters. Opioid and other neuromodulators	excitatory interneurons, glia, and other cell types.	(bidirecitional connections between widespread higher order cortical areas and the parahippocampal region, and between the parahippocampal region and the hippocampus); PFC and PPC interactions with multiple association cortices.	conjunction codes, up/down states, frontal/temporal coordinated oscillations, subsequent memory effect (fMRI, ERP)			
FOXP2; songbird work; mouse knockout work			Lateral superior and middle temporal cortices, inferior temporal cortex, inferior frontal cortex, inferior parietal cortex. Overlap with memory, motor, sensory, and emotional circuits	ERPs N400 (lexico-semantic and contextual processing; P600/late positivities (continued analysis); anterior negativities (language-related working memory)	Production and comprehension of words, coherent sentences, and coherent discourse (rating scales) Thought, Language and Commuinication Scale, Thought Disorder Index,		See narrative

Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-reports	Paradigms
LANGUAGE							
FOXP2; models based on songbirds; mouse knockout models			Language is mediated by networks distributed across lateral (including posterior superior and middle temporal), inferior temporal, anterior temporal, inferior frontal and inferior parietal (angular and supramarginal) cortices, which are often lateralized to the dominant hemisphere. Language comprehension and production can also engage other regions, including dorsolateral	N400 (indexing lexico-semantic processing in relation to preceding context and information stored within semantic memory), P600/late positivities (indexing continued analysis or reanalysis, often in response to conflict between levels of representation), anterior negativities (indexing working memory costs involved in holding and linking individual	The production and comprehension of words, coherent sentences, and coherent discourse.		*<u>A) Language Production:</u>* Naming Verbal descriptions of visual depictions of events and states Linguistic corpus-based analyses of language output. *<u>B) Language Comprehension:</u>* <u>1) Offline measures</u> The detection and classification of semantic relationships between words. The ability to distinguish between coherent and incoherent sentences and discourse. The ability to answer questions about the content of sentences and discourse. <u>2) Online measures</u> Listening and reading times to critical words and regions in linguistic input. Patterns of eye movements (in eye tracking paradigms) or motor movements (in mouse tracking paradigms) to critical words and regions in linguistic input. Patterns of eye movements to non-verbal visual stimuli during spoken language comprehension (the visual world paradigm).

			prefrontal and superior frontal and subcortical regions (cerebellum, striatum, thalamus). It can also engage the non-dominant hemisphere. These circuitries overlap with those mediating semantic, working, declarative and procedural memory processes. Some of the meaning extracted through language may be situated or embodied within motor, sensory and emotional systems and their underlying circuitries.	constituents within language).			Experimental Manipulations Manipulations of different types of relationships between individual words in priming paradigms. Manipulations of predictability and acceptability, at different levels of representation, in a linguistic input. Manipulations of different types of coherence and cohesion between clauses in discourse. Manipulations of relationships between language and non-verbal behaviors.

Genes*	Molecules	Cells	Circuits	Physiology	Behavior	Self-report	Paradigms
COGNITIVE CONTROL							
Component Process: Goal Selection, Updating, Representation and Maintenance							
			Frontopolar/ Anterior LPFC (BA10) Inhibition of DMN (?)			BRIEF (Gioa)	Badre tasks Koechlin paradigm Task Switching
COMT BDNF DISC1 5HT2A DRD4 DRD2 5-HTTLPR	Glu DA GABA NE AcH	Pyramidal PV	DLPFC PPC Thalamocortical	Gamma synchrony; pupilometry	Off-task behaviors; distractibility	Cognitive Failures Questionnaire (Broadbent et al) Disorganization Sx on SANS/SAPS/PANSS BRIEF (Gioa)	Task Switching (inc. Switching Stroop); AX paradigms; Cued stimulus-response reversal tasks; Tower tasks

Genes*	Molecules	Cells	Circuits	Physiology	Behavior	Self-report	Paradigms
Component Process: Response Selection, Inhibition or Suppression							
COMT CHRM4 BDNF DRD4	Glu DA GABA NE AcH	Somatostatin PV Pyramidal	DLPFC VLPFC PPC	theta gamma	Impulsive behaviors;	Disorganization Sx on SANS/SAPS/PANSS BRIEF (Gioa)	Simon Stroop Flanker
DRD4 DAT1 MAO-A 5-HTT	Glu DA GABA NE AcH	Pyramidal	Ventrofronto-striatal BA6/8 (FEF) Pre-SMA PPC	Alpha Pupilometry Short interval cortical inhibition (TMS)	Impulsive behaviors; off-task behaviors; distractibility	Conners impulsivity scale ADHD Rating Scale (Dupaul) BRIEF (Gioa) ATQ/CBQ Effortful Control	Go/Nogo Stimulus-Resp Incompat Stop-Signal Reaction Time Antisaccade Countermanding Conflicting and contralateral motor response task
							Motor persistence paradigms (e.g. NEPSY statue task)

Genes*	Molecules	Cells	Circuits	Physiology	Behavior	Self-report	Paradigms
<u>Component Process</u>: Performance Monitoring							
5HTTLPR	DA 5HT	-	ACC / pre-SMA Insula (?)	ERN N2 N450	Post-error or post-conflict adjustments in performance	YBOCS total score	Simon Stroop Flanker

* The Cognitive Control workgroup acknowledged that single gene findings are speculative, and may be misleading.

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