Mental Disorders, Computational Models of

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Mental disorders frequently disrupt cognition. Computational models are mathematical representations of cognitive or neural processes. These models have been applied to simulate cognitive deficits, to relate cognitive deficits to disturbances of neuroanatomy and neurophysiology, and to make predictions of the effects of brain disturbance on cognitive function.

INTRODUCTION

Psychiatric and neurological disorders are frequently accompanied by specific disturbances of perception, cognition, affect or motor control. In addition, these disorders have been associated with abnormalities of neuromodulation or neural connectivity, or loss of neurons. Computational models have been applied to simulate and predict human cognitive performance. More recently, computational models of neural circuit architecture and function have been used to relate cognitive deficits to neural abnormalities in specific disorders. (See Amnesia; Aphasia; Dyslexia; Memory Consolidation; Neurons, Representation in; Neurons, Computation in; Neural Development; Synapse; Hebb Synapse: Modeling of Neuronal Selectivity; Hebbian Cell Assemblies; Levels of Analysis in Neural Modeling; Learning and Memory, Models of; Attention, Models of; Neurotransmitters; Neural Degeneration; Synaptic Plasticity, Mechanisms of; Language Comprehension; Memory Models; Working Memory; Model Fitting)

Computational models have been instantiated at three general levels in mental disorders. Some models have focused solely on the cognitive level, and do not attempt to relate the architecture of the model to the neural substrates of a disorder (e.g. Carter and Neufeld, 1999). A second type of model has been motivated by the role of specific regions of the brain in cognitive disorders, or the role of a neurotransmitter in specific functions (Cohen and Servan-Schreiber, 1992; Haarmann et al., 1997). A third approach uses experimental studies of the properties of neurons and neural circuits in animals to design neural circuit simulations, and then lesion components of this neural model to determine how the lesion affects information processing within the circuit (Grunze et al., 1996; Hasselmo and Wyble, 1996). Most models have used neural network models to simulate mental disorders. Because neural network models employ an architecture of parallel, interconnected processing units which resemble the architecture of the nervous system, they may be better suited to modeling brain disorder than serial, symbolic programs with a single central processing unit. The distributed processing units in neural networks allow great flexibility in the level of implementation of the model. For example, processing units can represent the properties of individual neurons within a circuit, or abstract representations such as visual features or words. In this article, neural network models which attempt to capture the cognitive or biological features of several major mental disorders will be reviewed. (See Computational Models: Why Build Them?; Production Systems and Rule-based Inference; Connectionism; Connectionist Implementationism and Hybrid Systems; Backpropagation; Working Memory, Computational Models of; Neural Behavior: Mathematical Models; Semantic Networks; Spreading-activation Networks; Adaptive Resonance Theory; Language Learning, Computational Models of; Semantic Memory: Computational Models)

SCHIZOPHRENIA

Schizophrenia is a mental disorder characterized by cognitive deficits, hallucinations, delusions,
and disturbances of social and emotional behavior. Neuropathology suggests a reduction in neural connectivity, possibly secondary to abnormal synaptic pruning during development. In terms of neurotransmission, there is evidence of abnormal dopaminergic transmission, and of N-methyl-D-aspartate (NMDA) receptor function in schizophrenia. Notably, normal adults may develop transient psychotic symptoms similar to schizophrenia as a result of the use of amphetamines (which increase dopaminergic activity) or ketamine (a drug that blocks NMDA receptors). The application of neural network models has provided the first formal insights into the way in which these neural and cognitive features might be related (Grunze et al., 1996; Hoffman and McGlashan, 1997). Two models will be discussed here.

NMDA receptor function may be disrupted by schizophrenia. What would be the consequences of such a disturbance within local cortical circuits? At the circuit level, Grunze et al. (1996) studied the role of NMDA in modulating local circuit inhibition within the rate hippocampus. These neurophysiological findings were then used to develop a biophysical model to test the functional consequences of NMDA blockade. Grunze et al. found that inhibitory neurons in hippocampal circuits were highly sensitive to NMDA antagonists. Inhibitory neurons provide recurrent or feedback inhibition of the activity of excitatory, glutamatergic neurons. If NMDA receptors are dysfunctional in schizophrenia, recurrent inhibition would also be diminished, resulting in hyperexcitability within the circuit. A learning simulation using an auto-associative network showed that such a failure of recurrent inhibition would result in the spread of activation to irrelevant patterns during recall. This inappropriate spread of activation within a set of representations may contribute to such symptoms as ‘loose associations’ in speech, and disturbance of physiological measures of inhibition, such as P50 sensory gating and prepulse inhibition (Nestor and O’Donnell, 1998).

Dopaminergic neurotransmission is probably affected by schizophrenia as well. Dopaminergic modulation may play a role in prefrontal cortex maintenance of contextual information, and may affect gain in neural circuits. Cohen and Servan-Schreiber (1992) developed a back-propagation model of schizophrenic cognitive dysfunction which attempted to capture these features of schizophrenia, and they used the model to simulate deficits in task performance. The model had input, associative and output modules for learning. A context module affected the flow of information through the associative module. The context module provided functions similar to working memory (maintenance and manipulation of task-relevant information) and selective attention. Cohen and Servan-Schreiber found that reduction of gain in units in the context module resulted in degradation of internal representations in the context module. This may be analogous to the effects of dopamine dysregulation on prefrontal cortex function. The degradation of contextual modulation, in turn, resulted in deficits in network simulations of the Stroop task, the continuous performance test and a lexical disambiguation task. These simulated deficits were similar to those observed experimentally in schizophrenia. For example, individuals with schizophrenia show a bias towards the dominant meaning of a word, regardless of the prior context. Thus when provided with the prior statement ‘You can’t keep chickens’, followed by ‘without a pen’, patients with schizophrenia were more likely to say that pen referred to a writing implement rather than to a fenced enclosure. When the function of the context module was degraded by reducing gain of units in the context module, the model showed the same pattern of dominant response errors as subjects with schizophrenia. Figure 1 illustrates the network model for this experiment.

Although the Cohen and Servan-Schreiber model did not attempt to model at the level of neural circuits, it did demonstrate how a model may incorporate pathophysiological data into simulations of cognitive deficits, and it identifies mechanisms which may be responsible

![Diagram of connectionist model used in a lexical decision task implemented by Cohen and Servan-Schreiber (2001). The context module allows the system to disambiguate an input which could have either a dominant or a subordinate meaning. Decreasing the gain of the units in the context module produced a bias towards dominant meanings of an input, which was similar to the behavioral performance of patients with schizophrenia in lexical decision tasks.](image-url)
for behavioral deficits in superficially dissimilar tasks.

**HALUCINATIONS**

Auditory hallucinations are associated with a variety of mental disorders, such as affective psychosis and schizophrenia. Hallucinations are often characterized by hearing voices which an individual does not experience as his or her own, and which do not originate from auditory stimulation. In schizophrenia, such psychotic symptoms usually appear in adolescence or young adulthood, coinciding with the developmental interval in which large-scale synaptic pruning occurs in cortical areas. To investigate whether hallucinated speech could arise from pathological over-pruning, Hoffman and McGlashan (1997) developed a back-propagation network model of speech perception. The model had four layers, namely an input layer which represented phonetic features of words, a hidden layer that integrated feedforward projections from the inputs and recurrent projections from a temporary storage layer, a storage layer that represented working memory processes by storing a copy of previous hidden layer activation, and an output layer that represented semantic and syntactic features of words. To determine which word (if any) the model detected, output layer activation was passed through a decision algorithm. Before and after pruning, the authors counted the number of correct identifications, misidentifications and hallucinations for full, degraded and null (zero-valued) phonetic inputs. Hallucinations were defined as the presence of a detected word given a null input. Competitive pruning was modeled by modifying weights between the temporary storage and hidden layers.

Hoffman and McGlashan (1997) found that partial pruning of the network, which simulated normal developmental processes, enhanced the ability of the network to detect words. However, over-pruning impaired the network’s ability to detect words, and it produced stereotyped hallucinations. Although this simulation did not attempt to model speech perception at the level of neural circuits, it does support the neurodevelopmental usefulness of selective synaptic elimination. Furthermore, the model proposes a plausible developmental mechanism for schizophrenia that is consistent with morphological findings of decreased synaptic density and that predicts perceptual and working memory disturbances which are also found in the disorder.

**LANGUAGE DISORDERS**

Computational approaches have also been used to model disturbances of language processing caused by stroke. Classic theories of aphasia are framed in terms of the differential role of cortical regions. For example, left temporoparietal lesions often produce Wernicke’s aphasia, which is associated with severe language comprehension deficits. Computational models allow a formal representation of semantic and syntactic mechanisms that are affected by aphasia. Haarmann et al. (1997) postulated that left temporoparietal lesions cause sentence comprehension problems because they reduce the capacity of working memory for language. The authors tested this hypothesis in a hybrid computational model that combined the spreading activation of connectionist approaches with production rules (if..., then... statements). Their model contained three subsystems of production rules, namely a lexical access system, a parse tree system and a thematic role mapping system (Figure 2). The lexical access subsystem took the perceptual representation of single words as input, and activated word meanings, word syntax and verb structures as outputs. The parse tree subsystem applied grammar-based production rules to the syntactic output of the lexical access system to generate parse tree representations. Finally, the thematic role mapping subsystem combined word meanings and verb structures from the lexical system with parse tree representations to produce thematic role bindings (indicating who did what to whom). The performance of the model was determined by the activations of the thematic role binding units, which represented correct comprehension of parts of sentences. In the model, working memory capacity was defined as the total number of activation units that were available per unit of processing time. Activation spread at each processing step when conditions in the antecedent (if…) of production rules matched active elements in working memory.

In this model, aphasic performance was simulated by decreasing working memory capacity, or the amount of activation available per processing step. In situations where working memory demand (total activation summed across active antecedent conditions and production rule targets) exceeded capacity, target activations were reduced in order to maintain activations within the model’s capacity. This modulation of working memory capacity resulted in a pattern of performance that mirrors aphasic deficits. The model demonstrated forgetting (which was instantiated by below-threshold
activations), slower processing (which emerged because more processing steps were required to produce threshold activations) and partial comprehension (which corresponds to occasions when some processing steps never occurred because subthreshold activations did not engage production rules). These deficits closely resemble the patterns of forgetting, slower processing, and partial comprehension that are found in experimental studies of aphasia. The model also captures the interaction between sentence complexity and illness severity which is found in patients. Models with severely decreased working memory capacity performed like patients with severe aphasia – both showed progressively worse sentence comprehension performance with increasing sentence complexity.

ALZHEIMER DISEASE

Alzheimer disease is an adult-onset disorder associated with a progressive dementia. Initially, anterograde amnesia is the most severe deficit, but remote memories are also lost as the disease progresses. Neuropathological changes include loss of neurons and a reduction in cholinergic innervation of the cortex.

Hasselmo and Wyble (1996) used a neurophysiological model of pattern learning to show how cholinergic activity may play a central role in both the memory deficits and neural damage in Alzheimer disease. Within neural circuits, neurophysiological evidence and biophysical models suggest that acetylcholine suppresses association-fiber synaptic transmission, while direct afferent input remains effective. This allows learning of new patterns using the Hebb rule, while suppressing interference and runaway synaptic modification. If cholinergic activity was reduced, as occurs in Alzheimer-type dementia, the metabolic demands of the resulting runaway modification could result in the spread of neuronal damage and degeneration. Moreover, the functional consequences of excessive synaptic modification would include the disruption of learning and retrieval which has been observed in Alzheimer disease.

CONCLUSION

Computational models show promise for simulating experimental data and developing behavioral predictions with regard to cognitive processes in mental disorders. However, current models are limited due to their simplified representation of inputs, outputs and cortical circuits. The human cortex is estimated to contain billions of neurons, and each neuron may have thousands of connections. Current neural models typically use a small number of processing units and connection weights which cannot approach this level of biological complexity. In addition, because models have many parameters which can change as a function of initial weights, connections and learning, it is not clear how the fit of the model to experimental data or neural mechanisms can be rigorously tested. Nevertheless, the computational models
reviewed here often represent the first attempt to develop mathematical simulations of neural and cognitive deficits associated with mental disorders. The full potential of computational modeling of neural and cognitive systems may depend on the development of hardware and software which better represents the architecture of the brain.

References


Further Reading

