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Commentary

Can a Problem With Corollary Discharge Explain the Symptoms of Schizophrenia?

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Corollary discharge (CD) is a copy of a motor command that is sent to sensory regions of the brain. Such signals are a critical feature of the nervous systems of nearly all animals that can move. A primitive form of CD appeared almost as soon as self-propelled organisms evolved. The nematode *Caenorhabditis elegans*, for example, dedicates some of its 302 neurons to a CD circuit for inhibiting inappropriate reflexes triggered by its own movements. Animals that move need to be able to distinguish sensations caused by their own movements (reafference) from sensations caused by sources in the outside world. CD enables this distinction to be achieved. External sources of stimulation include the actions of other agents, and CD is a fundamental mechanism for distinguishing the self from the other.

A failure to distinguish the self from the other might underlie many of the positive symptoms of schizophrenia, such as delusions of control [Frith (1)], where one feels that one's own actions are being controlled by someone else. Irwin Feinberg (2) was the first to recognize that a defect of a CD mechanism might explain such symptoms. He discussed this possibility in relation to the disorders of thinking associated with schizophrenia, such as the experience that one's thoughts are not one's own (i.e., thought insertion). The idea that such positive symptoms can be understood in terms of CD mechanisms has been remarkably fruitful, generating a wide range of experimental studies that are reviewed in this special issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.

Circuitry

We now know far more about the various neural circuits underlying CD mechanisms.

There is no single type of CD circuit—rather, there are many subtypes depending on the sensory modality involved and the current motor plan. This becomes clear both when contrasting CD circuits in different species and when contrasting CD circuits associated with different sensory modalities in the same brain (3). For example, reafferent signals reaching the senses are canceled directly by motor signals (in crickets) or indirectly via intermediate brain structures (in mormyrid fish). Within the human brain, different circuits are associated with different modalities. At the level of the spinal cord, touch inputs are supressed while proprioceptive inputs are enhanced. The cerebellum plays a key role in reafference cancellation in the earliest stages of sensory processing, and motor inputs can also suppress reafferent sensory responses at the level of the cortex.

CD is an example of a mechanism by which one brain system updates another to coordinate the various stages in the control of current behavioral activity, and this is likely a general principle of brain function. Our brains are predictive, not reactive (4), and the concept of CD was an important precursor of the various computational models of predictive processing currently available. The predictive mechanism of CD can be reframed in terms of inverse and forward models. The inverse model calculates the movements needed to achieve desired goals; the forward model uses CD to predict the consequences of these movements. In the oculomotor system, the forward model enables us to have a stable perception of the world rather than fragmentary sensations created by eye movements. This is achieved by a circuit involving the superior colliculus, the medial thalamus, and the frontal eye fields. At a higher level, the same mechanism operates in decision making. When we make decisions, we predict outcomes and monitor to check how much predictions relate to actual outcomes. This process of prediction and self-monitoring guides future decisions. Here, a form of CD is operating in the cognitive domain.

Cerebellum

It has long been recognized that CD plays an important role in the functioning of the cerebellum. A major problem for the control of movement is caused by the inevitable delay in the arrival of the sensory feedback associated with movement. For example, there is a >100-ms delay before visual feedback indicates that a limb has arrived at its target. Prediction based on CD is used to overcome the destabilizing effect of this delayed feedback (5). Via various CD inputs, predictions computed in the cerebellum play a critical role in motor control and in sensory motor learning.

Cerebellar motor deficits appear to be a relatively frequent feature of schizophrenia, and they deserve more study (6). Similar failures of prediction are also characteristic of language production and comprehension in schizophrenia, but more evidence is needed to substantiate a role for the cerebellum in such higher cognitive functions.

Oculomotor Control

The best data available about the neural basis of CD come from the study of eye movements (7). There is also much evidence that abnormalities of eye movement control are associated with schizophrenia. Reduction in the accuracy of pursuit eye movements is one of the most robust findings in the literature on schizophrenia. In addition, greater severity of delusions is associated with reduced compensation for retinal motion during pursuit eye movements. As has been found previously with manual tasks, a reduction in error correction of

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eye movements in the absence of visual feedback is also associated with schizophrenia. All these examples of defects in motor control are consistent with disrupted CD, which in the case of oculomotor control may be a consequence of thalamocortical dysconnectivity. There is, however, a recurring issue with all attempts to explain the symptoms of schizophrenia in terms of these basic failures of CD mechanisms. Given the central role of CD in effective navigation through the world, shouldn't schizophrenia be associated with more profound impairments? And if the impairments are not so profound, how do they lead to the various debilitating, high-level symptoms associated with schizophrenia?

Monitoring of Speech

Certain positive symptoms of schizophrenia, such as auditory hallucinations, suggest that there has been a loss of the distinction between self and other in relation to speech. During speech—and indeed in all kinds of vocalization—the auditory system self-monitors for vocal errors while simultaneously maintaining attention to externally generated sounds. This self-monitoring is associated with the suppression of activity elicited by self-generated vocalizations. Studies of marmoset monkeys (8) have identified neurons in the auditory cortex whose activity is supressed in anticipation of self-generated vocalizations. These neurons also have a role in the feedback control of vocalization. The suppression of activity in auditory cortex depends upon a CD mechanism probably originating in brain areas that initiate or control vocalizations.

Speaking-induced suppression can also be reliably observed in humans (9), where it is marked by reduced amplitude of the N1 response in the electroencephalogram to self-generated speech. N1 suppression depends upon the predictability of the auditory signal. Suppression can also be observed for inner speech. Demonstration of this effect involves the use of an auditory probe that must be carefully chosen in relation to content and timing. These observations can be explained in terms of CD involving communication between the frontal and temporal cortices, while the cerebellum and the parietal cortex also have a role.

Speaking-induced suppression of activity in the auditory cortex is reduced in schizophrenia. This observation fits well with an explanation of auditory hallucinations and related phenomena in terms of a failure of CD processes in the auditory system. However, robust links with specific symptoms remain to be fully established.

CD and Psychosis

Evidence for CD mechanisms emerge early in human development. By 2 months of age, babies can discriminate between self-generated and externally generated stimulation (10). There is evidence that alterations of CD mechanisms can occur early in development and are associated with an increased risk of developing psychosis later in life. But how can these low-level problems with motor control eventually lead to the high-level positive symptoms associated with schizophrenia? Poletti *et al.* (10) make the interesting suggestion that the low-level problems with sensorimotor prediction could be increasingly experienced as a lack of control, leading to a weakened sense of agency in relation to the generation of actions and thoughts.

Feinberg's suggestion that the positive symptoms of schizophrenia reflect abnormalities of CD (2) has generated a substantial body of experimental evidence and theory, but the definitive story remains tantalizingly just out of reach. We have not identified the final common pathway in the brain that links the various CD circuits to the positive symptoms of schizophrenia, but as this special issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* demonstrates, we are in a strong position to move forward in this quest. New techniques are available for identifying CD circuits in the brain, and these can be complemented by computational models in a predictive coding framework. However, the most exciting developments are in the experimental techniques for studying some most elusive aspects of human behavior, such as inner speech and thought. These are the techniques we need if we are to understand symptoms as mysterious as thought insertion.

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Article Information

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