

Efference Copy, Corollary Discharge, Predictive Coding, and Psychosis

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About 40 years ago, Irwin Feinberg (1) suggested that failures of the efference copy/corollary discharge (EC/CD) mechanisms may underlie some of the symptoms of psychosis. This was followed by an elegant expansion of the theory by Frith (2) and supportive data by Shergill *et al.* (3). EC/CD mechanisms have been broadly described across the animal kingdom (4); they enable all animals that move to discount sensations that result from their own actions, thereby providing them with a sense of agency and allowing them to distinguish between the sensations arising from environmental stimuli and those arising from their own actions. Inspired by the writings of Feinberg (1) and Frith (2), we developed a neurobiological test of the EC/CD mechanisms using human vocalization (5), similar to that being used in nonhuman primate studies of these mechanisms (6–9), that could ultimately be used to test Feinberg's seminal hypothesis (1). Twenty years later, this continues to be the focus of our work and the nidus of this special issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.

Our intent was to publish articles that covered basic and clinical aspects of the various systems that relied on the EC/CD systems. We paired Thakkar and Rolfs (10) with Subramanian *et al.* (11) to review the literature on EC/CD during eye movements in the psychosis spectrum and the neural basis of the system from the nonhuman primate literature, respectively. We paired Whitford (12) with Eliades and Wang (13) to review the literature on abnormal suppression in people on the schizophrenia spectrum during vocalization and the neurobiology of auditory cortical suppression during vocalization in nonhuman primates, respectively. We paired Person (14) with Moberget and Ivry (15) to review the nonhuman and human literature, respectively, on the role of the cerebellum in the EC/CD system. Finally, separate but related contributions come from Poletti *et al.* (16) on the developmental trajectory of EC/DC systems and from Brooks and Cullen (17), who discuss variation in how such systems are neurobiologically instantiated, both across species and across modalities within species.

These contributions have been eloquently and succinctly summarized by Frith's commentary, for which we thank him. This frees us to elaborate on some themes of particular interest to us: our view of the sensitivity of the EC/CD systems to psychosis, psychosis vulnerability, and psychotic symptoms; the mixed and mixed-up use of EC and CD; and how predictive coding relates to EC/CD.

EC/CD Dysfunction and Psychotic Disorders

The major reason that EC/CD mechanisms are of particular interest in psychiatry is that dysfunction of such putative

mechanisms has the potential to fundamentally alter the way individuals experience the sensory consequences of their own actions, their ability to distinguish these sensations from those arising from environmental stimuli, their underlying sense of agency, and ultimately their experience of the world. While it is possible that EC/CD dysfunction could contribute to a variety of psychiatric symptoms, depending on the motor sensory systems affected, psychosis has been the dominant focus, starting with Feinberg's seminal article (1). There are at least two ways that EC/CD dysfunction could contribute to psychosis.

The first, emphasized by Feinberg (1) and later Frith (2), depended on persuasive arguments by John Hughlings Jackson (18) and others (19) that thoughts could be viewed as our most complex motor act, and that the EC/CD mechanisms that evolved to dampen the sensory consequences of our overt actions were conserved during the evolution of the mechanisms that support covert actions (i.e., thoughts). As noted by Feinberg (20), one reason to think that this might be true is that thoughts generate vivid percepts in the absence of external stimulation during dreams. This raises the possibility that EC/CD mechanisms associated with thought normally operate during consciousness to prevent thought-generated auditory experiences, while these operations are disabled during dreams. The view that EC/CD dysfunction contributes to psychosis through its operation on thoughts gave rise to relatively specific predictions about which psychotic symptoms would be affected. In particular, EC/CD dysfunction could lead to 1) auditory verbal hallucinations by failing to suppress sensory regions during the generation of thoughts, particularly unbidden thoughts, leading to their being perceived as externally generated, and 2) delusions of alien control due to misattribution of internal thoughts and experiences to external sources (1,2). Despite the compelling nature of this theoretical framework, it must be acknowledged that it remains largely an unproven conjecture that the EC/CD mechanisms that operate during motor acts like saccadic eye movements or vocalizations apply to thoughts. Demonstrating this convincingly is challenging because of the covert nature of thoughts. Indeed, it is for this reason that the paradigms used to document EC/CD dysfunction in schizophrenia spectrum disorders have used overt actions like vocalization, button presses, and saccadic eye movements. Although EC/CD studies have documented auditory cortical suppression during instructed inner speech (12), the intention to speak and the silent execution of speech are more similar to overt speech than to the unbidden thoughts that manifest as auditory verbal hallucinations or as confirmation of alien control of one's own

thoughts and actions. The hypotheses that these EC/CD abnormalities in psychotic disorders are reflections of broader EC/CD dysfunction operating at the level of thoughts cannot be rigorously tested until the proposition that EC/CD mechanisms operate on thoughts in a manner similar to other motor acts receives more direct empirical support.

The second way that EC/CD dysfunction could contribute to psychotic experiences is through the generation of “aberrant perceptual experiences” (21), wherein unremarkable or ignored sensory stimulation become perceptually salient (22). Efforts to account for these recurring perplexing perceptual experiences may then drive the generation and maintenance of delusional beliefs (21). To date, while EC/CD dysfunction has been demonstrated across the psychotic spectrum, clear demonstrations of correlations between the measured dysfunction and the severity of specific psychotic symptoms posited to arise from EC/CD dysfunction, such as auditory verbal hallucinations or delusions of alien control, are lacking, with a few exceptions (10,23–25). While there are a number of reasons that correlations with specific psychotic symptoms are challenging to demonstrate (26,27), it is also possible that EC/CD dysfunction may be more strongly linked to underlying feelings of perplexity associated with aberrant perceptual experiences than with specific psychotic symptoms, a hypothesis that remains untested to date. Moreover, the fact that abnormal EC/CD signals have been observed in attenuated form in the nonpsychotic first-degree relatives of psychotic patients (28) and in individuals with the psychosis risk syndrome (29) suggests that the EC/CD dysfunction may reflect the underlying vulnerability for psychosis and produce subtle perceptual alterations without actually driving the emergence or worsening of psychotic symptoms.

EC Versus CD

The terms “efference copy” and “corollary discharge” were independently coined to describe similar phenomena involving motor sensory feedforward signaling during execution of motor acts. Consequently, the terms are often used synonymously, and different investigators may use only one or the other in their published work (as is evident when surveying the papers in this special issue). Nonetheless, models of motor sensory feedforward signaling during action typically incorporate both the transmission of a copy of the motor plan from motor regions and a representation of the predicted sensory consequences of the motor act elsewhere in the brain (e.g., sensory cortices or cerebellum). For this reason, some investigators (30) use the term EC to refer to the former and CD to refer to the latter. Conceptually, it seems plausible that they could be distinguished, both temporally and neuroanatomically. Temporally, it can be argued that the generation and transmission of the EC should precede the actual initiation of the motor act, while the CD, or at least its comparison with the actual sensory consequences of the motor act (i.e., sensory reafference), arises subsequently to modulate the sensory response. For example, in our human electroencephalography studies during vocalization (23) and button pressing (31), we found that the strength of the neural activity immediately preceding the action (theorized to reflect the EC) predicted the degree of subsequent neurosensory suppression (theorized to

reflect the CD) during the action’s execution. Neuroanatomically, it seems that EC signals should be evident in motor regions where action plans are generated, while CD signals should be evident in sensory, cerebellar (14), and/or other regions involved in carrying out the comparison between the CD and sensory reafference produced by execution of the action. To date, much of the animal model research on EC/CD mechanisms record from just one brain region, limiting their potential to identify neurophysiologically distinct EC and CD signals. It remains unclear whether a distinction between the EC and CD can convincingly be validated at the neurobiological level, and some have argued that there is no distinction to be made (14). It seems to us there may be value in adopting the previously proposed conceptual distinction between the EC and CD in order to facilitate research on their neurobiological distinction (Figure 1).

EC/CD and Predictive Coding

Models of how the brain processes information have increasingly emphasized a predictive coding perspective, with the

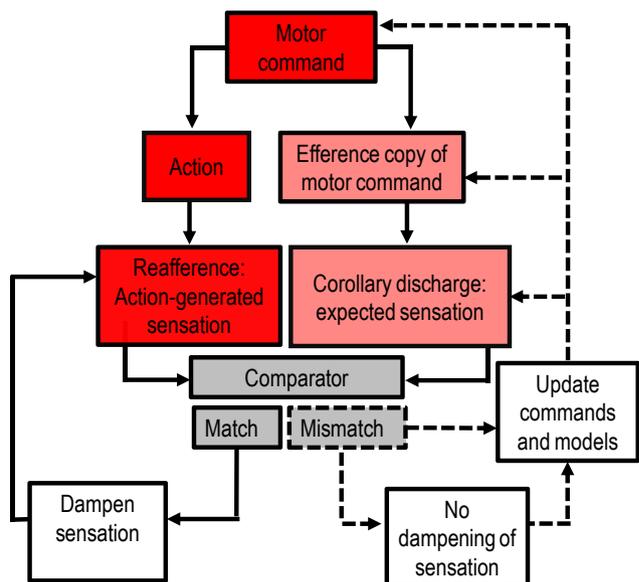


Figure 1. Conceptual distinction between efference copy and corollary discharge. As illustrated in the flowchart, motor commands (top red box) and ensuing actions (top left red box) are accompanied by transmissions of an efference copy of the motor plan from motor cortex (top right pink box), generating a corollary discharge of the expected sensory consequences (middle right pink box). The corollary discharge is then compared (middle gray box) to the real sensations, or reafference, resulting from the action (middle left red box). On the right (middle gray dashed lined box), a poor match sends an error signal (dashed lines) to the cortex to alter expectations or modify the action, as needed (lower right white box), resulting in little or no dampening of the sensation (lower right white box). On the left (middle gray solid lined box), a match results in a dampening or cancellation of sensation (lower left white box) in the sensory cortex (middle left red box). It is through this comparison process that errors are detected and corrected, before the proprioceptive system has a chance to respond and implement corrective action. This is likely carried out by automatic side-loops in the cerebellum (34), outside of conscious awareness. This system allows all species to fluidly and flexibly navigate the environment and discount sensations resulting from the movement.

brain constantly generating predictions about the environment and then dedicating neural resources to processing only stimuli that violate these predictions (i.e., prediction errors) in order to update predictive models of the environment. In some ways, the EC/CD mechanism can be thought of as just an action-based, specific case of predictive coding. However, one potential basis for distinguishing them is that context-based predictive coding encompasses learning to recognize and predict stimulus regularities in the environment, with prediction errors used to continually update the predictive model of the environment, whereas action-based predictive coding, as in the case with the EC/CD system, may involve more innate or hardwired modulation of sensory regions during motor activity required for distinguishing self from other while interacting with the environment. It is not clear whether the action-based EC/CD framework should be extended to more cognitive, less automatic actions, such as evaluating the consequences of decisions [as suggested by Subramanian *et al.* (11)].

Importantly, the predictive coding and EC/CD models of auditory verbal hallucinations seemingly make opposite predictions—on one hand, overreliance on Bayesian priors (i.e., predictions) is associated with auditory verbal hallucinations (32,33), while on the other hand, failure to predict self-generated sensations has been posited to be associated with experiencing auditory verbal hallucinations (1). These seemingly opposing views can be reconciled if deficient EC/CD drives (possibly compensatory) generation and maintenance of predictions about sensory events that are less susceptible to modification by prediction errors. Therefore, deficient EC/CD may result in the overreliance on predictions (Bayesian “prior probabilities”) that auditory events have occurred when they have not in individuals with auditory verbal hallucinations (33).

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