The function and failure of sensory predictions

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Humans and other primates are equipped with neural mechanisms that allow them to automatically make predictions about future events, facilitating processing of expected sensations and actions. Prediction-driven control and monitoring of perceptual and motor acts are vital to normal cognitive functioning. This review provides an overview of corollary discharge mechanisms involved in predictions across sensory modalities and discusses consequences of predictive coding for cognition and behavior. Converging evidence now links impairments in corollary discharge mechanisms to neuropsychiatric symptoms such as hallucinations and delusions. We review studies supporting a prediction-failure hypothesis of perceptual and cognitive disturbances. We also outline neural correlates underlying prediction function and failure, highlighting similarities across the visual, auditory, and somatosensory systems. In linking basic psychophysical and psychophysiological evidence of visual, auditory, and somatosensory prediction failures to neuropsychiatric symptoms, our review furthers our understanding of disease mechanisms.

Keywords: corollary discharge; efference copy; predictive coding; schizophrenia; hallucination

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Many aspects of our daily lives include navigating a changing and often unpredictable environment, in which we must correctly attribute agency and ownership to movements, actions, and their sensory consequences, discriminating them from environmental changes. For example, rotating the head to scan a large part of the visual environment causes image motion on the retina. How can the brain know that such motion signals are not due to physical object motion, but are instead triggered by head rotation? Our brain is equipped with mechanisms that allow us to resolve ambiguous signals, and to distinguish between external and self-generated sensory events. These mechanisms are vital to normal cognitive functioning because they help us predict the outcome of our own actions, and thus perceive self-generated events as nonalarming. Such predictive processes are the topic of this review.

The notion of our brain as an inferential machine that actively generates predictions of sensory inputs is a widely accepted view of perception that dates back to principles postulated by pre-Socrates philosophers and the seminal writings and observations of von Helmholtz: “Each movement we make by which we alter the appearance of objects should be thought of as an experiment designed to test whether we have understood correctly the invariant relations of the phenomena before us, that is, their existence in definite spatial relations” (von Helmholtz, 1878/1971, p. 384). The mechanisms underlying such active inferences in the sensorimotor systems are known as “corollary discharge (CD)” or “efference copy.” For nearly every movement we make, the motor system creates a copy of the movement execution command and sends it back to related sensory brain areas (visual, auditory, or somatosensory/proproprioeptive; Fig. 1). These internal feedback (CD) processes allow the brain to compare efferent (external) with reafferent (internal)
Figure 1. Basic feedback control model including sensory and motor processing pathways (black arrows) and feedback (red arrows). Sensory information is processed along modality-specific pathways and relayed to sensorimotor brain areas responsible for generating a motor plan. Movement generators (in brainstem/cerebellum) trigger a motor command, which is transmitted to the plant (e.g., the eye). Critically, a copy of the motor command (efference copy) is sent back to sensory and sensorimotor brain areas and integrates with the sensory input signal. Each movement also generates a change in sensory input (physical feedback).

signals, effectively resulting in the brain monitoring its own actions and predicting action consequences.

Across species, sensory receptors are indifferent to the source of their activation—whether a perceived visual event, sound, or touch is caused by the self or a potential predator. At a low processing level, intrinsic CD processes resolve this ambiguity by inhibiting inappropriate reflexive responses to self-generated sensations. At a higher processing level, they facilitate the analysis and interpretation of sensory information to enable cognitive functions such as sensorimotor learning and goal planning. Moreover, the ability to generate predictions about future events is critical for building an internal representation of the visual world, enabling perceptual stability. Such predictions also allow response monitoring, cognitive control, and learning. Computational and experimental evidence under the predictive-coding framework extends our understanding of how the brain constructs, maintains, and updates an internal model of the world and uses it to generate predictions about future sensory events. This theory of brain function assumes that the brain continually generates predictions based on current input and learned associations. In a recursive Bayesian process, predictions are compared with incoming sensory information, leading to the computation of an error signal, which the brain continually tries to minimize. Within this framework, CD signals could be seen as one of the key mechanisms underlying our ability to distinguish between self-generated and externally generated input. Along the same lines, the predictive coding framework offers a way of understanding the consequences of dysfunctions in the generation or transmission of CD signals. Such dysfunctions might underlie hallmark symptoms of neuropsychiatric disorders marked by cognitive dysfunction and psychosis. For example, positive symptoms of schizophrenia commonly include auditory hallucinations, linked to defective monitoring of speech production. Other symptoms of the disease that can be accounted for by the predictive-coding framework are passivity experience, for example, delusion of control—a patient feels that her/his actions are externally controlled—and general disturbances of the sense of agency—an inability to attribute one’s own thoughts, internal speech, covert or overt actions to oneself. Together, these symptoms may ensue from inadequacies in CD mechanisms across different sensory modalities, resulting in an inability to distinguish whether a sensory event has been self-produced.

This review will discuss the function of sensory predictive mechanisms across modalities and the consequences of failure of such mechanisms due to disease. In primates, CD mechanisms have been studied most extensively in the visual and oculomotor systems as the key mechanism underlying stable visual perception. Eye movement recordings, neurophysiological studies in monkeys, and psychophysical studies in humans have revealed the role of CD mechanisms in the ability to perceive a stable visual world across sequences of eye movements. In the auditory system, the ability to interpret one’s voice or inner speech as one’s own, as compared to hearing externally produced sounds, is likely the result of CD signals. Evidence for efference copy signals in the auditory system relies on electrophysiological and neuroimaging studies in humans revealing sensory attenuation or self-suppression—reductions in neurophysiological responses as a consequence of perceiving self-generated sensations as less salient. Similarly, in the somatosensory

system, CD signals allow us to interpret tactile stimulation as either self-induced or induced by others. Recent studies in neuropsychiatric populations have revealed striking deficits in CD function across modalities. For example, eye movement studies in schizophrenia have shown deficits in CD function affecting visual perception. These findings are paralleled by CD deficits in the auditory system, some of which have been linked to auditory hallucinations in schizophrenia.

Our review will focus on evidence supporting a sensory prediction failure hypothesis of perceptual disturbances associated with disorders such as schizophrenia. We will highlight experimental paradigms illustrating both the function and potential failure in sensory predictive mechanisms, central tenets of sense of agency. There are recent reviews covering aspects of CD failures, but these focus on individual sensory domains and are largely specific to symptoms of schizophrenia. Our review synthesizes evidence of CD function and failure collected across sensory modalities and attempts to generalize to other disorders involving prediction failure. CD mechanisms are ubiquitous across species, and much of our understanding of CD function relies on studies in animals such as mice or songbirds. Here, we focus on studies conducted in human and nonhuman primates with the goal of outlining implications of sensory prediction function and failure for our understanding of disease.

**Function of sensory predictions**

**Perceptual stability, continuity, and remapping in the visual system**

One of the most important predictive functions of CD for sensory processing is perhaps in maintaining perceptual stability across eye movements. When we shift gaze from one object of interest to another by making a fast saccadic eye movement, our percept of the visual environment is disrupted by a rapid sweep of the visual scene across the retina. Yet, despite these dramatic retinal image shifts, we usually perceive the visual world as stable and continuous, indicating that what we see is the result of an active constructive process or an internal representation of the world. Such internal representations are updated continuously with every eye movement through a mechanism known as remapping. In the saccadic system, remapping might be triggered by CD signals of the oculomotor command, signaling the intention to move the eye. Recordings from single neurons in brain areas, such as in the lateral intraparietal area (LIP) or superior colliculus (SC), where CD signals are believed to originate, revealed that these neurons can shift the locations of their receptive fields before saccade onset, effectively updating visual information in anticipation of the saccade’s retinal consequences (called predictive remapping).

Alternatively, remapping might reflect shifts of spatial attention toward a future target location as an effective mechanism underlying target selection, especially in areas such as frontal eye fields (FEFs), which play a crucial role in transmitting predictive signals to parietal cortex, and extrastriate area V4. The detailed temporal and spatial aspects of remapping and its relation to selective spatial attention have been investigated in neurophysiological and behavioral studies in nonhuman primates and in behavioral studies in healthy humans and patients. These studies focus on how we localize objects in the presence of a saccade.

One prominent way of assessing whether images are perceived as stable across saccades is through postsaccadic localization (Fig. 2). In such localization tasks, observers are required to make a saccade to a peripheral target. The target is extinguished during the saccade and reappears (either immediately or after a delay) at a displaced location; observers have to discriminate the displacement direction (e.g., to the right or left relative to the original target location). Humans are usually able to detect such target displacements with high accuracy, provided there is a blank period in between. This ability is thought to be facilitated by CD signals, compensating for saccade-induced retinal image motion. Interestingly, postsaccadic localization ability stays intact despite trial-to-trial variability of saccadic landing sites, and even when the saccade endpoint is manipulated through adaptation. These observations indicate that the CD signal incorporates saccadic errors and matches the planned upcoming saccade; it remaps the target to the expected postsaccadic retinal location.

The importance of CD information for remapping extends to updating a retinotopic map of attended locations, and their connections to other retinotopic areas (attention pointers). Such remapping of attention facilitates subsequent movements and...
perception at attended locations, and indicates the importance of CD function for higher level visual performance.

Another line of evidence comes from studies on peri-saccadic mislocalization (Fig. 2). When a visual target is briefly flashed at the time of saccade initiation, its location appears to be shifted in the direction of the upcoming saccade as if space was compressed toward the saccade target. This mislocalization usually occurs when visual targets are shown in darkness (i.e., in the absence of a spatial reference) and indicates that the oculomotor system preplans or anticipates the saccade, thus allowing the perceptual system to take it into account. However, effects of compression and suppression occur even in the absence of saccades, for example, when visual input is interrupted by masking. These findings imply the existence of a more general process that integrates and reconnects visual information across interruptions.

Additionally, CD information might underlie accurate motor performance in tasks that involve manipulating the saccade amplitude. In saccade adaptation tasks, a target is systematically shifted during saccade execution—either backward (toward the starting point) or forward (beyond the original target). As a consequence, the saccade system has to compensate by gradually adjusting saccade amplitude to the new target location. Behavioral studies show that such adaptations occur over the course of just a few minutes of practice, first by means of corrective saccades, and then by adjustments of the saccade amplitude. In tasks involving sequential saccades, such as the double-step saccade task, observers have to saccade to a series of two briefly flashed stimuli; here, the saccade system might rely on CD information to compensate for the sensory consequences of the first saccade. Saccade durations are generally so short that visual feedback or proprioceptive information cannot

<table>
<thead>
<tr>
<th>Modality</th>
<th>Experimental task and behavior measured</th>
<th>Performance / neurobiological measure</th>
<th>Measure indicating sensory prediction mechanism utilization</th>
<th>Measure indicating sensory prediction mechanism failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visual</strong></td>
<td>- post-saccadic or perisaccadic shift detection: perceptual localization via button press - double step: saccade adaptation - smooth pursuit: trajectory prediction</td>
<td>- saccadic end points, landing error - corrective saccade angles - smooth pursuit velocity gain, predictive acceleration</td>
<td>- perceptual judgments informed by sensory prediction independent of landing error - accurate second saccade in double-step - maintenance of pursuit during blanking; predictive acceleration; better prediction during pursuit than fixation</td>
<td>- perceptual judgments informed by landing error; greater difficulty in making perceptual judgments - inaccurate second saccades - reduced gain; no predictive acceleration; no pursuit benefit in prediction tasks</td>
</tr>
<tr>
<td><strong>Auditory</strong></td>
<td>EEG-ERP measurement during: - speaking - listening - inner speech - button press to elicit sound</td>
<td>- auditory cortex activity (N1 ERP component) during self- versus externally generated sounds</td>
<td>- attenuation / suppression of auditory cortex activity (N1) during self-generated sounds</td>
<td>- lack of attenuation in auditory cortex (no N1) during self-generated sounds</td>
</tr>
<tr>
<td><strong>Somatosensory</strong></td>
<td>self-generated tickle stimulus - participant reproduces force experienced</td>
<td>- reported level of “tickleness” felt by the foam - fMRI: brain activity during self-versus externally generated tactile stimulation - amount of force reproduced - fMRI: somatosensory cortex attenuation</td>
<td>- lower tickle rating in response to self-generated stimulation - activity reduction in somatosensory cortex / anterior cingulate gyrus with self-generated stimulation - overestimation of force when reproducing it</td>
<td>- no decrease in perceptual ratings for self-generated tactile stimuli - reduced / no somatosensory cortex attenuation - more veridical force matching (reduction in normal overestimation)</td>
</tr>
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Figure 2. Representative experimental paradigms measuring sensory predictive function and failure in the visual, auditory, and somatosensory system.
Table 1. Selected studies showing positive relationship between prediction failure and clinical symptoms of schizophrenia

<table>
<thead>
<tr>
<th>Modality</th>
<th>Study</th>
<th>Method</th>
<th>Paradigm</th>
<th>Evidence of prediction failure</th>
<th>Relation with clinical symptoms</th>
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</thead>
<tbody>
<tr>
<td>Visual</td>
<td>25,28</td>
<td>Eye tracking and psychophysics</td>
<td>Trans-saccadic perceptual localization task</td>
<td>Perceptual estimation relied on saccade end-point error; preserved saccade latency, amplitude, and variability; higher perceptual threshold</td>
<td>Correlation between perceptual bias and positive symptoms (PANSS) and sense of agency; no correlation between saccade metrics and positive symptoms</td>
</tr>
<tr>
<td>Visual</td>
<td>26</td>
<td>Eye tracking</td>
<td>Double-step saccade task, trans-saccadic perceptual localization task</td>
<td>Second saccade did not account for end-point error of first saccade</td>
<td>Correlation between error compensation performance and delusional ideation in healthy observers</td>
</tr>
<tr>
<td>Visual</td>
<td>27</td>
<td>Eye tracking and psychophysics</td>
<td>Perceptual prediction of motion direction during pursuit versus fixation</td>
<td>Equal perceptual performance during pursuit and fixation; preserved pursuit initiation, slowed velocity gain</td>
<td>Correlation between performance failure and PANSS global score, total symptoms, but not positive or negative symptoms</td>
</tr>
<tr>
<td>Visual</td>
<td>142</td>
<td>Eye tracking and psychophysics</td>
<td>Peri-saccadic perceptual localization task</td>
<td>Larger than normal mislocalization in the direction of the saccade</td>
<td>Dynamics of CD signal recovered by a model were correlated with symptom severity (BPRS)</td>
</tr>
<tr>
<td>Visual</td>
<td>146</td>
<td>Eye tracking</td>
<td>Pursuit tracking of a transiently blanked moving target</td>
<td>Lower predictive pursuit gain during blanking; preserved pursuit initiation (latency and acceleration)</td>
<td>Negative correlation between predictive gain and schizotypal-dimensional score in relatives</td>
</tr>
<tr>
<td>Visual</td>
<td>149</td>
<td>Eye tracking and psychophysics</td>
<td>Pursuit in front of moving background, judgment of background's motion</td>
<td>Background's perceived stationarity deviates from optimum of 0 relative to eye velocity (compensated reafference)</td>
<td>Stronger effects for patients with delusions of influence</td>
</tr>
<tr>
<td>Auditory</td>
<td>32,33</td>
<td>EEG</td>
<td>Speaking out loud versus listening to own played-back speech</td>
<td>Reduced increase of coherence between frontal and temporal lobes during speaking, same level as during listening</td>
<td>Strongest effects for patients with auditory hallucinations; inverse correlation of prespeech synchrony with auditory hallucination severity</td>
</tr>
<tr>
<td>Auditory</td>
<td>73</td>
<td>EEG, N100</td>
<td>Perceptual judgments of modified auditory feedback (own or other voice)</td>
<td>Less N100 suppression in response to own versus other</td>
<td>Scale for the Assessment of Positive Symptoms hallucinations score was correlated with the amount of N100 suppression in the left hemisphere</td>
</tr>
<tr>
<td>Somato-sensory</td>
<td>14</td>
<td>Psychophysics</td>
<td>Action recognition task; hand movements are fed back visually with spatial or temporal distortions</td>
<td>Higher error rates</td>
<td>Subgroup of patients with delusions of influence (SAPS) had higher error rates</td>
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Continued
be used to correct a saccade mid-flight. Instead, the saccade system is continually recalibrated by mechanisms adapting to changes in target location or amplitude. Interestingly, a similar recalibration of gaze appears to counteract instability during blinks, leading to effects akin to saccadic adaptation and revealing a potential role of CD mechanisms in perceptual stability across blinks. In sum, the ability to predict the sensory consequences of a saccade is crucial when planning sequences of multiple eye movements. Evidence for dynamic updating of predictions has recently been found in primary visual area V1, indicating that CD signals are fed back to the earliest stages of visual cortical processing.

Predictive mechanisms also play a substantial role in other types of eye movements, such as smooth pursuit—the eyes’ key response to visual object motion. Tracking a moving object with smooth pursuit leads to significant improvements in the ability to predict the object’s trajectory. This pursuit benefit was discovered using a paradigm in which observers had to extrapolate an object’s trajectory either while fixating, creating a retinal motion signal of the moving target, or during smooth pursuit, triggering a combination of retinal and extra-retinal CD signals. Congruently, studies that involve tracking a disappearing and reappearing target—akin to tracking a cat that disappears behind a tree and then reappears—have revealed signatures of predictive mechanisms, modulated by activity in frontal brain areas such as FEF.

Typically, when parts of a target trajectory are transiently occluded, smooth pursuit eye movements can be maintained, but only up to about 1 s, and at a reduced velocity. Importantly, when the time of reappearance is held constant, observers predictively accelerate their eye movements before the target’s reappearance, thereby reducing the accumulating velocity error. Pursuit maintenance during transient absence of visual input and predictive acceleration of the eye could be achieved by a CD mechanism, in which the only available input is an internally generated efference copy of the eye movement command.

To summarize, CD signals relay saccade and pursuit eye movement metrics such as onset, direction,
amplitude, and speed to the perceptual system via a pathway from SC to frontal and parietal cortical areas, thereby enabling sensory predictions.

**Recognition of self-produced sounds in the auditory system**

Similarly, the ability to recognize self-generated auditory stimuli, such as speech, from externally generated sounds is vital for processing the myriads of auditory stimulation we experience at any instant. Consistent with CD function in the visual system, cortical areas dedicated to speech production send efference copies of self-generated speech sounds to auditory cortex, where sounds are perceived. Parallel to the visual system, such CD mechanisms would then enable predicting the onset of self-generated overt speech (and arguably covert, inner speech). Efference-copy function in the human auditory system has been established through studies showing reduced auditory cortical responses to self-generated as compared to externally generated sounds. Most of these studies rely on electroencephalography, magnetoencephalography, or neuroimaging (Fig. 2). For example, auditory cortical responsiveness can be assessed with the N100 (N1), a large negative component of the auditory event-related potential (ERP), peaking about 100 ms after the onset of a sound. The N1 amplitude is commonly found to be reduced in response to spoken (self-generated) as compared with playback vocalizations.\(^{69–73}\) This response attenuation or self-suppression has been found to originate in primary auditory cortex.\(^{20,22,74,75}\) Evidence for multimodal sensory attenuation comes from functional MRI (fMRI) studies\(^{76,77}\) showing that bimodal action consequences led to the suppression of the blood oxygen-level dependent (BOLD) response in a broad network, including bilateral auditory and visual cortices, and enhanced the detection of delays between action and feedback, compared to unimodal action consequences. These findings indicate that action-related predictive mechanisms might lead to suppression in multiple modalities. However, direct evidence for attenuation of cortical activity in the visual domain is sparse; indeed, some studies have revealed increased visual cortical activity following self-initiated actions in humans\(^{78}\) and awake-behaving mice\(^{79}\) potentially indicating differential processing of self-initiated sensory stimuli across modalities.

Overall, reductions in auditory cortical responsiveness are congruent with findings obtained by invasive methods in human neurosurgery patients,\(^{20,71,72}\) and with results obtained using neuronal recordings from the auditory cortex in unrestrained marmoset monkeys.\(^{22,80,81}\) In all these cases, auditory responsiveness was reduced or suppressed when the animal was actively vocalizing. Interestingly, findings of auditory response attenuation extend to situations in which articulation is silent. When healthy individuals were asked to silently articulate a sequence of words or imagine the sequence with no overt articulation during functional imaging, a left hemisphere network implicated in speech production was activated during both tasks.\(^{82}\) Investigating whether inner speech also triggers the production of an efference copy and sensory attenuation is challenging when using electrophysiology, because inner speech does not elicit a measurable ERP. To bypass this problem, participants were visually cued to produce a single phoneme in inner speech at a specific point in time, coinciding with a matching or nonmatching sound played simultaneously via headphones. Inner speech produced similar suppression of auditory cortical activity (N1) when the produced phoneme matched the audible one, revealing that inner speech produces efference copies even in the complete absence of an overt motor act.\(^{83}\)

Suppression of auditory cortical activity has also been observed for sounds that were self-elicited via manual button press\(^{30,32,84,85}\) (Fig. 2) versus when the same sounds were either temporally predictable (cued) but not self-generated, or not predictable at all.\(^{32,86}\) However, N1-suppression can occur at a reduced magnitude even when auditory stimulus onset and frequency were unpredictable, indicating that predictive model mechanisms can withstand uncertainties in the frequency and onset of sound occurrence.\(^{87}\)

Although studies investigating action-related auditory ERP modulations mostly report response diminishations, it is plausible that certain task settings may result in activity enhancements. For example, increased BOLD activity in auditory cortex was reported during self-generated motor sequences that produced tones (e.g., playing on a piano keyboard) as compared with externally generated tones; human observers also had lower hearing thresholds for self-generated sounds.\(^{88}\)
Importantly, the same study found attenuation in frontal regions (such as superior and middle frontal gyri) in response to the same stimuli, indicating that self-generated sounds can lead to both reduced and enhanced cortical activity, depending on the brain region. The authors interpret these findings in terms of the relationship between the motor effector used to generate the sound (the hand), and suggest that a CD signal sent from motor cortex enhances activity in auditory cortex, increasing perceptual sensitivity. Moreover, auditory cortex activity enhancement was found in areas contralateral to the sound-producing hand, while the largest monaural sensitivity increases were found ipsilateral to the sound-producing hand. These findings imply strong lateralization and reveal some of the cortical connectivity of CD signals in the auditory system. They also show that movements other than vocalizations can modulate activity in auditory cortex. Finally, this study draws attention to the fact that CD signals can excite activity in sensory cortical areas, potentially via reafferent feedback. This interpretation is congruent with findings obtained at the single neuron level, revealing activity changes that evolve dynamically over time: While the majority of neurons in auditory cortex exhibit reduced firing rates at around 200 ms before self-vocalization onset, a small subset of neurons increased firing rates at around the time of vocalization onset.²²

In summary, suppression of auditory cortical activity in response to self-produced versus externally generated sounds provides evidence for the presence of a predictive mechanism originating in motor/speech production areas, potentially mediated by CD signals. Our review focuses on studies conducted in humans and monkeys, but it is important to note that CD mechanisms producing inhibition of auditory areas during self-induced sound, such as singing, are present across species, for example, in songbirds or crickets.³⁷,⁸⁹–⁹² Moreover, CD signals are not only critical for the discrimination of self-produced versus externally generated sounds, but they also enable higher level functions such as learning of acoustic behavior, speech, and music across species by suppressing auditory responses to movement-related stimulation.⁹³,⁹⁴ Auditory cortical neuron attenuation has been observed at the single-cell and circuit level using optogenetics in mice,⁹⁵ providing important tools for our understanding of neural circuit dysfunction in diseases such as schizophrenia.⁹⁶,⁹⁷

**Recognition of self-produced tactile sensations in the somatosensory system**

Parallel to findings obtained in the auditory system, activation in somatosensory cortex increases in response to externally generated touch and decreases in response to self-initiated touch.⁹⁸,⁹⁹ Congruently, predictive mechanisms in the somatosensory system enable differentiations between one’s own expected actions and those that are external and unexpected.¹⁰⁰–¹⁰² In a classic experiment demonstrating this principle,⁹⁹ human subjects were asked to move a stick device that stroked a piece of foam over their palm, either instantaneously or with a short delay (Fig. 2). The stimulation felt most ticklish when the temporal delay was large. This observation indicates that the extent to which self-produced tactile sensations are felt to be reduced (i.e., are nonticklish) is proportional to the error between predicted sensory feedback, based on an internal forward model of the motor system, and actual sensory feedback, produced by the movement.

Congruently, self-generated tactile stimuli produce diminished activity in somatosensory areas, indicating that the system must be able to accurately predict consequences of touch actions, such as when we attempt to tickle ourselves.⁹⁸,¹⁰⁰ Behavioral and imaging studies suggest that the origin of such an inhibitory input signal to somatosensory cortex might be in the cerebellum. For example, the right anterior cerebellar cortex responds to external tactile stimulation. But, it is selectively less active in response to a self-initiated movement that results in a tactile sensation versus a movement that does not result in a sensation. These findings suggest that this cerebellar area discriminates movements depending on their sensory consequences and might be involved in generating a CD signal that dampens down activity in somatosensory cortex, where tactile sensations are processed.¹⁰³,¹⁰⁴

Another important function of CD signals originating in the cerebellum is the facilitation of higher order mechanisms related to motor learning and control.¹⁰¹–¹⁰⁴ How we adapt movements in response to error may depend in large part on our expectations about the sensory feedback that our movements produce. Visuomotor adaptation
paradigms are a common methodological approach to investigate how humans modify behavior in response to misalignments between the intended and actual movement. Current predictive-coding models of adaptation postulate that the sensory consequences of a motor command are predicted based on internal action-related information, and that motor behavior is modified based on predictive processing.\textsuperscript{103–107}

In summary, there is converging and overlapping evidence for predictive signal-driven sensory modulation across modalities: remapping activity to maintain stability across saccades and to enhance perception in the visual system, attenuation or enhancement of cortical activity in response to self-generated sounds in the auditory system, and activity diminution in response to self-produced tactile stimuli in the somatosensory system. These parallels indicate that the observed movement-induced modulatory activity might reflect a general property of sensory systems, at least across the auditory and somatosensory system. Sensory feedback-based predictions might underlie our sense of agency,\textsuperscript{108} such that mismatches between our expectations and feedback lead to a reduced sense of action ownership.\textsuperscript{109}

Through predictive processes, our sensory systems are able to monitor their performance, assessing whether motor plans for eye or body movements, touch or speech unfold as intended, and modifying them when error sets in. Thus, sensory prediction is crucial for processing the overwhelming stream of external input, rapidly remapping spatial and attended locations, and reducing cognitive load by attenuating sensory processing of signals that result from our own actions.

**Failure of sensory predictions**

*Inhibition deficits in the auditory system and auditory hallucinations*

When sensory predictive functions are impaired, our sense of agency—of owning and controlling our thoughts, overt and covert speech, and action—is perturbed. Nonattributed or misattributed thoughts and actions are perceived as delusional or hallucinatory. Such failures in sensory predictive coding across modalities have been linked to symptoms of psychosis (Table 1), most prominently to auditory hallucinations and cognitive delusions, two of the hallmark symptoms of schizophrenia. Many of the characteristic features of the disorder (e.g., passivity experiences—“somebody else is controlling my actions,” thought insertion—“somebody is putting their thoughts into my head,” and auditory verbal hallucinations—hearing voices in the absence of a speaker) might arise from abnormalities in predicting the sensory consequences of self-generated actions.\textsuperscript{9,11,109}

According to this perspective, auditory hallucinations result from a breakdown in the awareness of self-generated action, apparent during speaking and inner speech. Auditory experiences, coupled with an inferential bias based on prior beliefs,\textsuperscript{110,111} or delusions about the source of inner speech, are perceived as voices coming from sources other than the self.\textsuperscript{35,112–115} More specifically, according to the predictive-coding theory, hallucinations would be triggered by attributing more weight on prior beliefs and expectations—top-down influence of prior knowledge—and by relying less on sensory signals—bottom-up sensory evidence—as a result of CD failure. Recent studies suggest explicitly that auditory hallucinations could be triggered by overweighting of prior information.\textsuperscript{110,111} This view is congruent with studies on perceptual inferences providing evidence for strong priors in patients with schizophrenia\textsuperscript{116} that might be related to symptoms of cognitive delusions.\textsuperscript{117}

Several lines of empirical evidence support prediction failure as the mechanism underlying auditory hallucinations. Auditory cortex activity attenuation or self-suppression in response to self-generated sounds is markedly reduced in schizophrenia\textsuperscript{33,69,118},\textsuperscript{118} and self-suppression could be a potential mechanism underlying auditory hallucinations. In these experiments, patients and healthy participants were instructed to either speak aloud or listen to prerecordings of their own speech. In healthy listeners, a CD signal is presumably generated in frontal cortical areas responsible for speech production and relayed to temporal cortex,\textsuperscript{70} where it suppresses activity related to the reception of auditory stimuli (as measured by the N1). The transmission of the CD signal is reflected in neural synchrony across brain areas before speech onset, and in an increase in neural activity coherence between frontal and temporal areas in the speaking condition. Two key findings have been observed in patients with schizophrenia: first, the coherence of neural activity across frontal and temporal areas did not differ between the speaking and passive
Moreover, patients showed a diminished perceptual ratings of self-produced tickle sensation as compared with healthy controls. Importantly, these findings extend to nonclinical individuals in the general population who have high schizotypy scores. Inability to attribute a movement or action to oneself versus another is also related to dysfunctions in self-monitoring, that is, in predicting the sensory consequences of one’s own actions. Evidence for this assumption comes from a study in which patients and healthy controls were asked to reproduce a target force exerted on their left index finger by pressing back with their right index finger (Fig. 2). All participants overestimated the required force, presumably because the sensory consequences of self-generated actions were predicted and taken into account—self-generated forces are generally perceived as weaker than externally generated forces. Interestingly, patients’ force matching ability was more veridical than healthy observers’ performance, reflecting a failure of the sensory system to attenuate the somatosensory representation related to the sensory consequences of the action. In line with this finding, neural activity in somatosensory brain areas was decreased in response to self-generated actions in healthy controls, as expected, but not in patients with schizophrenia. These impairments in self-monitoring and source attribution and the lack of attenuation of somatosensory activity may account for pervasive sensory abnormalities in schizophrenic patients, altering the experience of their own overt and covert actions, as well as their sense of agency and interactions with the environment. The demonstrated failure to appropriately translate and modulate generated motor force in patients with schizophrenia might also give rise to motor symptoms, such as problems with the timing of somatosensory responses. Importantly, motor symptoms are found in medicated as well as drug-naïve patients and their nonpsychotic first-degree relatives, and can therefore not be considered a side-effect of antipsychotic medication alone. For example, a study comparing brain activity in response to self-generated versus externally generated tactile forces found increased activation in somatosensory brain areas when the force was self-generated in patients with schizophrenia as compared with healthy controls. Such increased correlations between force intensity and sensorimotor brain activation in schizophrenia might reflect a sense of agency and interactions with the environment. The demonstrated failure to appropriately translate and modulate generated motor force in patients with schizophrenia might also give rise to motor symptoms, such as problems with the timing of somatosensory responses. Importantly, motor symptoms are found in medicated as well as drug-naïve patients and their nonpsychotic first-degree relatives, and can therefore not be considered a side-effect of antipsychotic medication alone. For example, a study comparing brain activity in response to self-generated versus externally generated tactile forces found increased activation in somatosensory brain areas when the force was self-generated in patients with schizophrenia as compared with healthy controls. Such increased correlations between force intensity and sensorimotor brain activation in schizophrenia might reflect a

Inhibition deficits in the somatosensory system and sense of agency

Reduced modulation of somatosensory activity in patients with schizophrenia would result in an inability to predict and cancel self-produced relative to externally produced sensations. Schizophrenia patients with positive symptoms (passivity and/or auditory hallucinations) exhibited increased per-
lack of response attenuation during self-generated movements.

Abnormal sensorimotor processing in schizophrenia extends to the use of external/visual performance feedback. Observers were asked to point at visual targets in a virtual reality set-up, and then to provide a visual estimate of their own movement direction. Importantly, observers received distorted visual feedback about their movement outcome, rotated around the actual movement. Individuals with schizophrenia showed difficulties in perceiving distorted visual feedback and relied extensively on the false external agency cue when estimating their pointing direction. These impairments in the ability to classify and correctly utilize (or ignore) external feedback indicate deficits in action attribution or ownership—abilities mediated by cerebellar circuits—and were correlated with patients’ scores in positive symptom assessments (Table 1).

Congruent with these results, patients with schizophrenia also show evidence of abnormal action recognition. In a task in which an image of a virtual right hand holding a joystick was presented to observers through a mirror, such that the image was superimposed on their real hand holding a real joystick, people with schizophrenia had more recognition errors in identifying the hand as virtual versus as their own. Error rates were particularly high when temporal delays and angular perturbations were randomly introduced when subjects had to perform joystick movements, such that the movement of the virtual hand deviated from the movement executed by observers.

Taken together, evidence from the tactile, visuomotor, and force processing domains of somatosensory function indicates that efficient utilization of a sensory prediction mechanism is crucial to maneuver within the environment. When sensory prediction mechanisms fail, as seen in neuropsychiatric disorders like schizophrenia, disturbances in action inference and modulation, agency attribution, and processing of self-versus-other sensations ensue.

**Compensation deficits in the visual and oculomotor system**

In the healthy oculomotor system, CD signals enable a stable percept of the visual environment. They provide an internal reference signal—the efference copy of the eye movement command—which can be subtracted from retinal signals to yield the percept of a nonmoving visual world during eye movements. This can be achieved by remapping either the entire visual field, or by updating only attended areas of the visual field, such as those around the future (attended) saccade target as a sparse and efficient way of remapping attention pointers. When CD signals are impaired or absent, the world can be perceived as instable during self-generated movements, resulting in perceptual errors and illusions. For example, placing the finger at the lower eye lid and gently pushing one’s own eye ball upward creates a distinct percept of downward motion. This erroneous motion percept emerges because retinal image displacements are not compensated by efference-copy signals; these signals are only available to cancel out displacement when eye movements are generated actively. The importance of such healthy compensation mechanisms is revealed by studies in patients. Following bilateral extrastriate cortex lesions, a patient reported perceiving motion of the stationary environment at a velocity corresponding to his own eye movements; he also reported severe vertigo whenever his eyes were in motion. Intact smooth pursuit eye movements and motion sensitivity in this patient point at an involvement of higher order visual processing areas, for example, along the occipito-frontal-parietal network, in integrating CD signals with retinal motion information.

Similar misperceptions and perceptual estimation errors have been reported in patients with schizophrenia across oculomotor tasks, and have been attributed to CD failure. In the pursuit system, patients showed deficits in a task that involved predictive judgments about object motion trajectories during pursuit versus fixation. When asked to estimate whether a visual object (the “ball”) would intersect with a line segment (the “goal”) in a task in which both objects disappeared before intersection, patients’ overall estimation performance was not impaired as compared to controls. However, patients did not benefit from tracking the ball with smooth pursuit eye movements, whereas controls showed a significant pursuit advantage as compared with performing the same task during fixation. These findings indicate that healthy controls generate and use an efference copy of the pursuit command to inform their perceptual judgments, resulting in higher estimation accuracy.
By contrast, patients were either unable to generate, relay or integrate this signal with the ball's retinal motion signal. It is important to disentangle such perceptual performance deficits from known deficits in visual motion processing and pursuit eye movements in patients with schizophrenia, where impairments have been reported at every stage of the sensory and oculomotor processing network. Early visual processing dysfunctions are well documented and often involve dorsal stream regions such as medial temporal cortex, the brain’s key motion processing area. Impaired motion processing cascades into deficits in smooth pursuit eye movements—reduced ability to match eye velocity to target velocity (low velocity gain) and to track a moving object smoothly (increased number of catch-up saccades). These pursuit deficits are among the most robust behavioral findings in schizophrenia. However, patients in the motion trajectory estimation study showed reduced pursuit gain, but relatively unimpaired pursuit initiation, indicating intact visual motion processing. Their lack of pursuit benefit therefore indicates a failure to effectively use information derived from sensory predictive mechanisms.

Similar CD failure has been demonstrated in localization tasks performed in the presence of saccadic eye movements. In peri-saccadic localization tasks, patients with schizophrenia make larger errors localizing a secondary target flashed at the time of the saccade than healthy controls. Interestingly, patients made localization errors in the same direction as healthy controls but patients’ errors were larger, indicating that a CD signal was generated in these patients, but was inefficient/over damped (started earlier and lasted longer). In trans-saccadic shift detection tasks, a target is horizontally shifted while subjects are asked to make a saccade. Congruent with findings in other localization paradigms, schizophrenia patients were less accurate than controls and appeared to rely more on saccade end points than on the actual physical target location. Such increased reliance on saccade end points and variability of performance might reflect deficits in remapping shifted targets, potentially triggered by CD signal disruption. In line with these findings, schizophrenia patients had greater difficulty in detecting target location shifts.

In studies of sequential saccades requiring adaptation, as in the double-step paradigm, schizophrenia patients were slower in their adaptive response and made fewer and smaller corrective saccades. Further, their corrective saccades were biased in the direction that would be expected if they were moving their eyes directly from the first to the second target, even when the actual first saccade fell short of or overshot the target. These findings indicate failure in using CD to predict the change in eye position resulting from the first saccade when executing the second saccade.

The discovery of efference-copy or CD failure exhibited in the pursuit and saccadic system of patients with schizophrenia fits well with known deficits in predictive eye movements in these patients. Such disturbances have probably been demonstrated most extensively in paradigms involving the extrapolation of visual motion trajectories when an object was briefly blanked from view. In such blanking paradigms, smooth pursuit can only be maintained in the absence of a visual target by relying on extraretinal motion signals—efference copy signals or velocity memory signals. Schizophrenia patients and their first-degree relatives robustly exhibit lower pursuit gain in the absence of a visual target. Similar findings were obtained when a pursuit target was stabilized on the fovea so that no retinal velocity signal was available and pursuit had to be internally driven. These findings indicate both an overall inability to predict future events, as well as a failure to use extraretinal motion signals such as efference copy; they have frequently been associated with brain areas responsible for the generation of predictive or anticipatory eye movements in frontal cortical areas, such as the FEFs.

In sum, these predictive deficits support the assumption that schizophrenia patients may have difficulty compensating for sensory (retinal) consequences of their own eye movements parallel to findings obtained in patients with bilateral cortical lesions. They are also congruent with the assumption that patients over-rely on retinal error signals to maintain stable pursuit or to perceive visual target displacements. Importantly, in several of these studies, perceptual deficits congruent with CD failure were related to assessments of subjective sense of agency or positive symptoms (Table 1) and to delusional traits in healthy individuals. Parallel to findings obtained in the auditory and sensorimotor system, studies
in the oculomotor system therefore emphasize the link between CD function and symptoms of psychosis.34,35

**Neural correlates of corollary discharge function and failure**

Models of neural mechanisms underlying CD function incorporate brain areas responsible for the generation of motor commands and for the processing of sensory input. Even though general principles of connectivity are similar across modalities, the specific areas involved—parietal cortex, prefrontal and temporal areas, thalamic nuclei, cerebellum, and their disseminated patterns of activity—differ between the visual, auditory, and somatosensory system (Fig. 3).

The neural circuits responsible for controlling visually guided eye movements and the generation and integration of CD information are well understood as a result of extensive work in nonhuman primates4,16,18,19,152–154 and are outlined in Figure 3A. The CD pathway originates from the intermediate layers of the SC, through the medial dorsal nucleus (MDN) of the thalamus, to the FEF. The FEF then transmits predictive signals to posterior parietal lobes (e.g., LIP) via feedback connections. Posterior parietal areas send signals about the actual visual input back to FEF via feed-forward connections (not shown).

Accordingly, in tasks requiring localization across saccades, neural activity related to remapping can be found extending from striate area and extrastriate visual cortex to SC, MDN, LIP, and FEF.4,16,152–154,156,157 Recent studies have focused on the microcircuitry in area FEF as a key structure underlying saccadic remapping.158 The importance of FEF has also been recognized in stimulation studies in humans, showing that transcranial magnetic stimulation over frontal cortical areas (FEF homologue) impaired visual stability across eye movements.159 Deficits in double-step saccade tasks in patients with thalamic lesions43,46 further emphasize the importance of these brain structures for CD function. Deficits in sensory prediction could arise from failures in generation, transmission, or utilization of CD signals (Fig. 3A). At the generation node, motor neurons in SC may fail to produce a CD signal, or may produce one that does not relay adequate information about the eye movement. Alternatively, structural or functional impairments in MDN could hinder receipt or onward transmission of signals to FEF, thus affecting remapping responses and subsequent relay of remapped information to visual areas. In schizophrenia, sensory prediction failure in the visual system might be associated with disruptions along the SC-MDN-FEF route, and this assumption is supported by neuroanatomical and imaging studies. Neuroanatomical abnormalities in thalamic MDN of schizophrenia patients include significant reductions in volume or neuron count and diminution in glucose metabolism.160–162

Considering MDN’s vital role in communicating between distinct associative cortical areas, these alterations likely lead to connectivity dysfunctions such as compromised cortical–MDN connections.163–165 Deficits in predictive eye movements in schizophrenia point to impairments in FEF, a structure that is critically important for the generation of predictive responses, and likely involved in the integration of retinal and extraretinal (efference copy) signals and in the transmission of these signals to parietal areas.18,63 These abnormalities could disrupt the critical CD pathway and represent the neural basis of the deficits described above.

Within the auditory system, an efference copy of articulation-related actions encodes expected sensory consequences of speech (Fig. 3B). Articulation-related motor planning originates in frontal cortical area and subsequent motor commands are sent from primary motor cortex (M1) to respective muscles for speech production. Efference-copy signals are simultaneously sent to auditory cortex, where they are integrated with auditory reafferent signals (postarticulation sensory feedback and speech sounds). Expected and actual postarticulation feedback signals are compared, thus attenuating activity in primary auditory cortex in response to self-generated sounds. Auditory hallucinations have been associated with abnormalities in primary auditory cortical function. For example, auditory hallucinations produce activity in auditory cortex at the cost of processing external sounds.166 Congruent with findings in thalamic MDN in the visual and oculomotor system, smaller volume of anterior/middle superior temporal gyrus (auditory cortex) was associated with the severity of auditory hallucinations in schizophrenia;167,168 these areas also contained morphologically abnormal pyramidal cells.169 Bilateral gray matter abnormalities were observed...
in middle and posterior segments of the temporal lobes, including superior temporal gyrus. Abnormal connectivity between cortical areas identified in auditory tasks includes both hyper- and hypoactive connections between Heschl’s gyrus and frontoparietal as well as hippocampal regions and between cortical hemispheres in schizophrenia patients with auditory hallucinations (Fig. 3B).
In the somatosensory system, efference-copy signals likely emanate from premotor structures and are utilized by anterior cerebellar cortex to generate internal predictions of tactile feedback (Fig. 3C). The association of anterior cerebellar cortex with primary and secondary somatosensory cortex activity, and its role in processing anticipated versus unanticipated somatosensory stimuli is well established. Discrepancy between predicted outcome and reafferent feedback (e.g., incongruency resulting from delayed or externally generated somatosensory feedback) produces an increase in activity in bilateral secondary somatosensory cortex, right anterior cerebellar lobe, and anterior cingulate. However, self-produced movements that trigger tactile stimulation result in decreased cerebellar activity. The activity of the cerebellum thus modifies the parietal cortical responses, conceivably through trans-thalamic pathways. In schizophrenia, hyperactivity in the inferior parietal lobule is associated with difficulty detecting discrepant proprioceptive feedback. The cerebellum partakes in nonmotor as well as motor functions, and it has been postulated that somatosensory abnormalities in schizophrenia may stem from cerebellar dysfunction or disconnection.

Reduced cerebro–cerebellar connectivity in higher level association networks, and increased cerebro–cerebellar connectivity in networks implicated in self-referential, spontaneous mental activity. Such connectivity abnormalities, in conjunction with abnormalities in cortical and thalamic structures, regional metabolic aberrances, and abnormal neural synchrony, could give rise to the experience of self-agency in the context of predictive somatosensory and motor control function (Fig. 3C).

**Unifying neural correlates of prediction failure across sensory modalities**

Notwithstanding the involvement of different brain areas and pathways in prediction function and failure in the visual, auditory, and somatosensory system (Fig. 3), some general principles can be observed. First, across sensory modalities, prediction failure seems to be related to connectivity dysfunctions along the thalamic-cortico-cerebellar route. Such large-scale connectivity disruptions, assessed via brain-wide functional connectivity analysis, might also underlie positive symptoms in schizophrenia. Specifically, the thalamus seems to have decreased connectivity with the cerebellum but increased connectivity with sensory cortical areas (e.g., occipital and temporal). Together, these observations point to a significant role of the thalamus in the pathophysiology of schizophrenia. Second, and in line with observed connectivity dysfunctions involving the thalamus, significantly reduced volume and metabolism have been observed in this brain area.

To conclude, we postulate that breakdown in sensory prediction mechanisms is likely the result of impaired transmission of CD signals to respective areas within affected networks. The following evidence supports this conclusion: (1) patients with schizophrenia who suffer from auditory hallucinations show impaired patterns of neural synchrony across brain areas; (2) neuroanatomical abnormalities—reductions in volume, metabolism, and neuron count—in thalamic MDN of schizophrenia patients might underlie connectivity dysfunctions between thalamus and cortex; (3) and deficits in predictive eye movements and saccadic remapping indicate dysfunction in area FEF, a brain structure that receives input from MDN and is critically involved in further transmitting integrated sensory, motor, and efference copy signals to parietal brain areas. Such transmission problems could include patterns of temporal disorganization with aberrant functional connectivity and erroneous spatial dissemination of these signals that underlie specific perceptual and cognitive states and cause disintegration of information across specialized brain areas in patients with symptoms related to prediction failure.

**Clinical significance for psychosis and related symptoms**

A large focus on research in predictive function and failure has been on patients with schizophrenia. This disease is associated with abnormal perceptions, a skewed conception of reality, and an array of emotional and cognitive impairments. Notwithstanding the interpretational complexity intrinsic to studying a heterogeneous disorder such as schizophrenia, this review presents converging evidence supporting a sensory prediction failure hypothesis of perceptual disturbances in schizophrenia across different sensory modalities. Importantly, psychophysical and neurophysiological evidence from experimental paradigms across modalities associates sensory...
prediction failure with disease symptoms such as hallucinations and cognitive delusions (Table 1). This research therefore has several important implications for our understanding of schizophrenia in particular and of psychosis in general.

First, robust evidence of CD failure has been observed in patients as well as in their first-degree nonpsychotic relatives and in the continuum of psychosis, irrespective of medication status. These paradigms might have the potential to reveal early markers of the disease, thus enabling earlier diagnosis and treatment. Importantly, recent studies have accumulated evidence that connectivity dysfunctions may be a vulnerability, or trait, marker of psychosis as well as a biomarker of psychotic illnesses themselves; they are also present in the continuum of psychosis, that is, clinical high-risk youth, nonpsychotic individuals with schizotypal personality traits, and in first-degree relatives. These findings suggest that connectivity dysfunctions, as well as related CD failures, might be linked to vulnerability, rather than the disease itself. Future studies could examine the link between abnormal connectivity and CD failure in the schizophrenia spectrum.

Second, there might be considerable overlap between the brain pathways underlying CD mechanisms and the disconnection framework associated with schizophrenia. This framework assumes that schizophrenia could arise from dysfunctional integration of a distributed network of brain regions as a result of impaired neuronal plasticity and its contribution to shaping the connections and dynamics that underlie brain function. Schizophrenia has been considered to be associated with structural and functional brain connectivity reductions that are evident even before disease onset. Neurobiological underpinnings such as cortico-thalamocortical communication and neuronal loss in thalamic nuclei (e.g., MDN) in schizophrenia are consistent with findings demonstrating CD failure in this disease. Importantly, brain areas such as the thalamus and FEF, both critically involved in CD function and failure, provide potential future avenues for developing novel antipsychotic targets or neuromodulatory treatment of drug-resistant auditory hallucinations in schizophrenia. Finally, prediction is a canonical process in the brain, with separate but partly overlapping networks underlying CD function in different modalities (Fig. 3). However, converging evidence points at prediction failures across modalities in schizophrenia. These findings could either indicate dysfunctions in long-range connections between brain regions, rather than in specific brain areas. Alternatively, it is possible that subgroups of patients exhibit modality-specific CD failure. Studies are needed that examine CD failure across modalities in the same group of patients to address this question.

Research paradigms and models that highlight the function and failure of sensory predictions also lend themselves to the growing area of computational psychiatry. Modeling data from such paradigms (e.g., eye movements, motor systems, and auditory system) may lead to identifying distinct disease subprocesses or patient subgroups. In the specific case of schizophrenia, a caveat is that the sensory predictive processing framework may not provide an account of negative symptoms, or explain why symptoms differ so markedly from patient to patient, producing highly variable psychosocial and functional outcomes. CD mechanisms must be related to other clinical and neurocognitive deficits associated with schizophrenia to ultimately allow the development of diagnostic tools and therapeutic interventions for perceptual and cognitive abnormalities. Moreover, whereas this review has largely focused on schizophrenia, it is important to note that some of the clinical symptoms associated with CD failure, such as hallucinations, are common in other diseases as well. For example, visual hallucinations frequently occur in patients with vision loss (Charles Bonnet syndrome) and are also increasingly becoming recognized as pervasive symptoms of Parkinson disease. However, little is known about CD function in either of these groups of patients. At the same time, motor symptoms, a hallmark of Parkinson disease, are now becoming recognized as an important research domain in schizophrenia. Abnormalities in dopaminergic and GABAergic pathways are associated with both diseases, and comparative studies of CD function and failure in these groups of patients could enhance our understanding of disease pathophysiology. This review provides a framework for future studies.
of CD function and failure across modalities and clinical populations.

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Competing interests

The authors declare no competing interests.

References

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