Review

A cognitive regulatory control model of schizophrenia

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A R T I C L E   I N F O

A B S T R A C T

A puzzling aspect of schizophrenia concerns the relationship between negative and positive symptoms. Perspectives suggesting that they arise from the same pathophysiological process are not consistent with the numerous differences such as treatment response, and the underlying neurochemistry relevant to treatment. Explanations viewing negative and positive symptoms as independent processes or diseases cannot readily account for the typical developmental course of schizophrenia, consisting of a lengthy prodromal phase of negative followed by positive symptoms. A model of schizophrenia is presented positing that negative and positive symptoms are distinct but interrelated processes, with the former bringing forth the latter due to damaged or impaired cognitive regulatory control processes. The extensive cognitive distortions, thought form variants, and sensory perceptual experiences comprising psychosis represent a natural propensity derived from the evolution of human intelligence. To facilitate reality congruency typically necessary for adaptive functioning, cognitive regulatory control processes normally prevent these extreme variants from entering the conscious and awake state. During sleep when there is no need for reality congruency the cognitive regulatory control processes are deactivated and psychotic equivalents are expressed. Psychological defensive functioning can also deactivate these processes and allow psychosis to manifest. The negative symptoms of schizophrenia are seen as arising from diverse neural deficits that impair to varying degrees the cognitive regulatory control processes, thus producing psychosis. The pattern of neural damage determines the negative symptom profile, and the impact on cognitive regulatory control processes influences whether negative or positive symptoms dominate or exist in relatively equal proportions.

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Contents

1. Introduction

Schizophrenia consists of both positive and negative symptoms [18,28,56]. Positive symptoms are known as psychosis with extensive alterations of thought content (delusions), thought form, and sensory perceptions (hallucinations). Negative symptoms include absence states, basic cognitive deficiencies, and social cognitive impairments. Absence states consist of apathy, amotivation, avolition, anhedonia, alogia, motor retardation, affective blunting and absence of play and curiosity [7,63]. Basic cognitive symptoms largely consist of deficits in executive functioning including cognitive flexibility, working memory, planning, attention, response inhibition, and multitasking [10,26,48,69,77]. Social cognitive symptoms involve diminished social drive and so-called Theory of Mind deficits, referring to impairments in how people think about themselves, others, social situations and interactions [29]. Using longitudinal criteria a particularly stable and enduring subset of these negative symptoms referred to as the deficit state has been identified, including restricted affect, diminished emotional range, poverty of speech, reduced interests, diminished sense of purpose, and diminished social drive [2,18,51,56].

The division of schizophrenia into positive and negative subtypes is justified on the basis of: symptom profiles, course of

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illness, response to treatment, underlying neurochemistry relevant to pharmacological treatment, structural and functional neurobiology, neuropsychological functioning, family history, premorbid adjustment, and risk factors [17,27,44,52–54,57,64,83,85]. For example, response to treatment and neurochemistry underlying pharmacological treatment demonstrate radical differences between positive and negative symptoms. In response to antipsychotic medication psychosis typically resolves rapidly and fully leaving negative symptoms still present [1,2,5,33]. On the other hand, negative symptoms tend to persist and are extremely resilient to treatment, major efforts producing limited gains [1,16,23,65]. For example, Dickinson et al. [23] found that extensive cognitive remediation training failed to produce a significant benefit on any neuropsychological or functional outcome measure.

In regards to the neurochemistry underlying pharmacological treatment, antipsychotic drugs resolve psychosis via blockade of dopamine 2 (D2) receptors, an action characterizing all antipsychotic drugs [33,74,88]. Negative symptoms instead involve alternative neurochemical targets including various serotonin receptors, such as 5HT-1A and 5HT-2A, glycine and glutamate (NMDA receptor subtype), and medications improving negative symptoms act on these alternative targets [33,37,38,41,45,58]. Further supporting the distinction between positive and negative schizophrenia, positive symptoms are not associated with neuropsychological deficits, and negative and cognitive symptoms are much more correlated than are positive and cognitive symptoms [10,39,62,78]. When psychosis remits cognitive impairments persist consistent with neuropsychological deficits lacking an association with psychosis [21].

Despite the vast body of knowledge acquired, a major gap in our understanding of schizophrenia concerns the relationship between positive and negative symptoms. As to how negative and positive symptoms relate to one another three general categories of explanation have been proposed: they arise from a single pathophysiological process, there are a number of separate such processes, and there are different diseases involved [50]. The latter two categories of explanation are similar in that they consist of separate and independent processes or diseases, as opposed to a unitary process producing diverse manifestations. Although the perspective that schizophrenia arises from a single pathophysiological process might seem most parsimonious, the vast number of differences between positive and negative symptoms [10,17,27,39,44,52–54,57,62,64,78,85] makes this category of explanation untenable.

There are also problems with the view that schizophrenia arises from separate and independent pathophysiological processes or diseases, based on the temporal course of the disorder. If positive and negative symptom categories are truly independent we would expect to see them arising without any consistent pattern. For example, both occur at the same time, or positive symptoms occur first followed by negative symptoms at approximately the same frequency as the reverse. In contrast to this random pattern what is seen is a very different scenario—schizophrenia typically begins with a lengthy prodromal phase of negative symptoms and declining functioning often lasting for several years followed by positive symptoms [25,27,40]. How might we understand the relationship between positive and negative symptoms based on the typical pattern of negative symptoms preceding positive symptoms? A fourth category of explanation consists of positive and negative symptoms arising from different pathophysiological processes and being linked, with one bringing forth the other. Based on the typical temporal sequence it is posited that the neural process underlying negative symptoms brings forth positive symptoms.

2. A cognitive regulatory control explanation

Extensive neural impairments occur in schizophrenia [26,27,38,40,57,64,69,85], and there are features of both a neurodevelopmental and neurodegenerative disorder [38]. These neural impairments seem to account for the diversity of negative symptoms given the extensive and varied changes in structure and functioning that occur [38,50,57,63,64,85]. Positive symptoms are postulated to arise from a very different process, namely as a natural extensive of the cognitive capacities provided by the evolution of human intelligence. Far surpassing that of even our closest cousins the great apes, intelligence evolved in humans to such an extent that we are able to design and master complex technologies, problem solve in a conceptual way, function and communicate in complex social groupings, and become the top predator with very limited natural body weaponry [6,55]. Derived from these cognitive capacities are an extensive range of thought content, thought form, and sensory perceptual experiences.

Cognitive distortions (thought content) range from mild to extensive [12,13,80]. Milder variants of a positive nature include placing a self-enhancing spin on events and seeing things through rose-colored glasses. Moderate versions produce excessive fantasy involvement, magical thinking, and over-valued ideas. More extensive cognitive distortions cross the border into the realm of actual psychosis, namely delusions [12,13]. In regards to thought form a natural range occurs extending from highly logical thinking to loose associations, circumstantiality, tangentiality, blocking, and derailment [12,13]. As a natural course of events some people are tighter in their thinking and others looser. Furthermore, the thought form of even a tight thinker can become circumstantial, tangential, or blocked at times, underscoring the potential range of expression. The intensity and quality of sensory experiences also vary within the general population, and hallucinations are actually very common such as with those arising in the transition between sleep and waking states, during grieving reactions, and in otherwise completely healthy people [46,59,72,81].

Given the presence of psychosis in the general population and in common grieving reactions, it certainly appears that the human brain is vulnerable to psychosis. Indeed, a capacity for psychosis seems to be present in us all—"The central nervous system appears to possess a latent capacity, neurobiologically speaking, for a pattern of functioning, which experientially is human psychotic consciousness," [11]. This capacity exists on a continuum as opposed to an all or none process [19,82]. Underlying this innate capacity is our naturally occurring range of thought content, thought form, and sensory perceptual experiences. An interesting and highly familiar demonstration of the naturally occurring range of these cognitive parameters is provided by dreams. Cognitive distortions often more bizarre than the delusions encountered in schizophrenia are routine, and the form of thought is frequently extremely loose, vague, and tangential. Strange sensory perceptions are common such as faces changing shape or people turning into monsters. In addition, we seem to hear voices and bizarre sounds while dreaming, and hypnagogic and hypnopompic hallucinations constitute extreme sensory perceptual alterations transpiring just upon going to sleep and waking, respectively [20]. More mild to moderate variants of thought content, thought form, and sensory perceptual experiences also occur, but dreams are where our extreme variants of these cognitive capacities express themselves.

If psychotic equivalents are a normal part of sleep and we have a natural capacity for psychosis why does it not manifest in most people during the conscious and awake state? To facilitate reality congruency, typically necessary for adaptive functioning, more extreme and less reality congruent cognitive distortions, thought form variants, and sensory perceptual alterations must be blocked

by cognitive regulatory control processes when a person is awake and conscious. During sleep there is no need for reality congruency and the cognitive regulatory control processes are deactivated. It is hypothesized that the neural changes underlying the negative symptoms of schizophrenia damage or impair the cognitive regulatory control processes, allowing more extreme cognitive distortions, thought form variants, and sensory perceptual experiences into the conscious and awake state on a routine and persistent basis. Adaptive functioning in general depends on cognitive regulatory control processes preventing reality incongruent behavior from being expressed. Schizophrenics frequently display bizarre and inappropriate behaviors demonstrating unregulated expressions of urges, impulses, wishes, and emotional reactions.

Certain other conditions where psychosis transpires can understandably involve defective cognitive regulatory control due to neurological impairments, such as dementia, delirium, and some states of addiction and withdrawal. In the case of bipolar disorder cognitive regulatory control processes blocking both psychosis and the conversion of hypomania to mania can be impaired or damaged, accounting for the co-occurrence of psychosis and mania. Excessive activation of the limbic system has been associated with schizophrenia and psychosis in particular [3,84], possibly due to impairment of the relevant cognitive regulatory control processes allowing over-activity of the limbic system and the emergence of psychosis. A perspective regarding auditory hallucinations, potentially applicable to other forms of hallucination, consists of inner speech being 'heard' as coming from an external source [30]. Based on this perspective cognitive regulatory control processes normally deactivate the auditory cortex allowing inner speech to be appreciated as coming from within. When these processes fail the auditory cortex is active during inner speech and it is perceived as coming from an external source producing an auditory hallucination [30].

A plausible candidate for the site of these cognitive regulatory control processes is the prefrontal cortex. Supporting this notion is the involvement of the prefrontal cortex in cognitive control generally [70], and inhibitory control over inappropriate or maladaptive emotional and cognitive behaviors [24,61]. For example, Lhermitte et al. [61] found that patients with frontal lobe deficits impulsively act on immediate cues without any inhibition of detrimental behavior. Further support is derived from the role of the prefrontal cortex in dreaming: the prefrontal cortex is less active during dreaming [79], and the bizarreness of a dream is directly related to the degree of hypofunction of the prefrontal cortex (Hobson et al. [43]). There is evidence that the prefrontal cortex undergoes extensive changes during schizophrenia that could damage or impair the functioning of cognitive regulatory control processes residing there [32,68,69,76,86,87]. Hence, neural impairments giving rise to negative symptoms likely damage or impair cognitive regulatory control processes, allowing reality incongruent behavior of diverse forms to routinely intrude into the conscious and awake state.

3. Discussion

A potential limitation of the theory proposed pertains to the notion that positive symptoms involve cognitive deficiencies much as do negative symptoms—neural damage associated with schizophrenia might cause the cognitive changes present in both positive and negative symptoms without evoking cognitive regulatory control process functioning. Several cognitive problems have been identified as being associated with psychosis such as a probabilistic reasoning bias for delusions [36], distorted attribution biases [8], preferentially seeking specific information such as threat related [47], interpretations of aberrant perceptions [22], altered representations of the mental state of others [31], and jumping to conclusions [34]. Research does show that those

with delusions demonstrate attribution and probabilistic reasoning biases [8,35].

The cognitive changes characterizing psychosis essentially consist of distortions, often with increased mental activity. Reasoning processes are biased, attributions are distorted, certain specific types of information are preferentially sought influencing decisions, active interpretations of aberrant perceptions are made, representations of the mental state of others are altered, and conclusions are jumped to often involving the linkage of unrelated data points. In contrast, the cognitive changes associated with negative symptoms entail diminished abilities and frequently reduced mental activity, due to deficient executive functioning [2,10,18,26,48,50,51,56,69,82]. Hence, the cognitive changes characterizing negative symptoms are qualitatively different than those present in psychosis, consistent with two separate processes.

In addition to explaining how positive and negative symptoms of schizophrenia relate to one another, the cognitive regulatory control process model can help in our understanding of the variable symptom range in schizophrenia, and why psychosis occurs in contexts where damage or impairment to the cognitive regulatory processes seem unlikely. Regarding the first matter, the diverse nature of the neural damage associated with schizophrenia influences the pattern of negative symptoms that manifests [4,9,31,38,60,63,64,66,69,76,84,86,87]. These diverse pathological changes might also have differential effects on the cognitive regulatory control processes such that the impact can range from minor to major. If there is only minor impairment to the cognitive regulatory control processes then negative symptoms greatly exceed positive ones and negative type schizophrenia dominates. If the cognitive regulatory control processes are heavily hit then there will be intense damage or impairment to them, and positive symptoms will dominate over negative ones. These two extremes might account for negative and positive forms of schizophrenia, with a mixture being more common.

To account for psychosis in contexts where damage or impairment to cognitive regulatory control processes is unlikely, psychological defense mechanism functioning is important to consider. Psychosis is common in grieving reactions and in the general population [20,46,72,81]. Hallucinations frequently occur with bereavement [72]. For example, an evaluation of 293 widowed people found that 14% had a visual hallucination of their deceased spouse and 13% experienced an auditory hallucination [72]. Furthermore, 47% had the more general hallucinatory event of experiencing the presence of the deceased spouse. Hallucinations are also quite normal in the general population, such as with vivid dream like hypnagogic and hypnopompic hallucinations [20]. The prevalence of hallucinations in the general population is between 10% and 25% [46]. In this context hallucinatory experiences tend to be positive and self-limited [81]. So common are hallucinations that a social movement has even formed to promote the normalcy of such behavior [81].

While damage or impairment to the cognitive regulatory control processes can understandably cause psychosis in the case of most mental illnesses, its presence in grieving reactions and the normal population is not so straightforward. For example, if defective cognitive regulatory control was responsible for psychosis during grieving reactions, we would expect it to be expressed in a non-specific random fashion involving delusions, thought form alterations, and diverse hallucinations occurring in roughly equal proportion. Instead, what is encountered is much more specific, namely hallucinations of the lost person's sound, sight, and presence [72]. These sensory experiences seem to be compensating for the lost sensory and related emotional input strongly demonstrating defensive compensation. Perhaps it is the case that deactivation of cognitive regulatory control processes naturally occurs in conjunction with sufficient defensive motivation in order to facilitate

these responses. Partial or full deactivation of the relevant cognitive regulatory control processes routinely occurs during sleep, indicating that there is flexibility in their application.

Psychosis certainly does seem to be motivated by psychological defensive processes in the case of grieving reactions. Defensive motivation also seems to apply, at least to some extent, with delusional disorder and paranoid personality disorder. The delusion basis of these disorders constitutes an extreme version of a normal defensive process, cognitive distortions [12,13]. With delusional disorder and paranoid personality disorder an entire system, as opposed to an isolated delusion, is constructed in a self-defensive fashion. For example, with paranoid delusional systems negative qualities are projected onto others, meaning that only positive qualities are seen as characterizing the self. To lose this system typically means that the person loses their defensive armor entirely and often their very purpose for being [14].

With both delusional disorder and paranoid personality disorder it is possible to imagine both damaged or impaired cognitive regulatory control processes and psychological defensive motivation. What might best fit with this co-occurrence is a spectrum ranging from brief defensive deactivation and no damage/impairment, to extensive damage/impairment and no defensive function, of the cognitive regulatory control processes. Schizophrenia occupies a position close to the latter end of the spectrum, psychosis in the context of grieving occupies the defensive end, while delusional disorder and paranoid personality disorder involve both defensive deactivation and some element of damage/impairment to the cognitive regulatory control processes. Psychosis occurring in response to stress further illustrates how this spectrum applies, in that some instances such as those entailing severe physiological stress arise primarily from impairment to cognitive regulatory control processes, others mainly from psychological defensive functioning, and still others from both mechanisms.

Delusional cognitive distortions and hallucinations expressed in the conscious and awake state can and do perform a defensive function in certain contexts, but what about for schizophrenia? Damaged or impaired cognitive regulatory control processes allow psychosis to manifest, so any defensive action would have to be after the fact involving an unconsciously motivated application. In some instances delusions seem to be structured to give meaning to a life that has largely lost its sense of purpose, as occurs with many schizophrenics. For example, a belief that federal agents are seeking you because you hold key information provides some measure of importance. Psychological processes are able to influence the content of delusions, as evidenced by self-esteem being a powerful determinant of how self-enhancing delusional content is [15]. This process accounts for why delusions are ego-syntonic given that they are consistent with a person's self-perspective.

Although much more speculative, psychosis might also be capable of partially offsetting reduced cognitive and emotional activity resulting from negative symptoms, despite its reality incongruent and dysfunctional aspects. Some of the neural structures and advanced connectivity damaged in schizophrenia appears to have allowed for the enormous cognitive and social advances of our ancestors [67]. Consistent with this perspective, genes conferring vulnerability to schizophrenia significantly overlap with those implicated in the evolution of human-specific cognition [49]. Given both their relatively recent evolutionary origin [49,67] and complex nature, the underlying neural structures and connections might be vulnerable to failure during development. Even just based on their highly ordered and complex nature, a certain frequency of maturation failure is to be expected derived from entropy considerations (highly ordered structures are difficult to maintain and there is a natural propensity for them to decay into disorder). Damage to the neural structures providing for human specific cognition,

and the resulting negative symptoms, would likely have been very fitness reducing during our evolution. Monkeys with frontal lobe ablations show severely impaired social functioning reminiscent of the deficit state of schizophrenia and often die isolated after being chased from the group [71].

Psychosis could potentially compensate by both providing extra cognitive activity directly derived from the more extreme cognitive distortions, thought form variants, and sensory perceptual experiences, and indirectly from the strong cognitive and emotional reactions occurring in response to the various psychotic manifestations. Even a slight fitness advantage in the context of negative symptoms could help explain the persistence of schizophrenia in the population. In support of this speculative and after the fact so to speak defensive role of psychosis, schizophrenics with positive symptoms tend to fair substantially better over time than schizophrenics with only negative symptoms [25,42,63,65,73,75]. In addition, schizophrenics with only negative symptoms demonstrate much greater overall behavioral rigidity than do schizophrenics with prominent psychotic symptoms [25,42,83].

Novel approaches to schizophrenia in terms of research investigations and treatment follow from this cognitive regulatory control model. Regarding research, genetic and structural–functional investigations need consider: first, negative symptoms as arising directly from neural damage; second, psychosis as a natural propensity representing the extreme point on a range of thought content, thought form, and sensory perceptual experiences; third, the role of cognitive regulatory control processes in blocking these extreme variants from the conscious and awake state. This approach differs radically from a focus on one common pathophysiological mechanism. Treatment approaches can be tailored to address dysfunction in the cognitive regulatory control processes. For example, pharmacological agents might be designed to compensate for damage or impairment to these processes, and non-pharmacological approaches might be devised to strengthen them. From a more humanistic perspective the model narrows the gap between normality and psychosis, given that the difference hinges largely on cognitive regulatory control processes that are routinely deactivated during sleep. Clinicians might then feel less different from psychotic patients, thereby facilitating greater rapport and hopefully improved treatment compliance.

4. Conclusion

In the model presented the extensive cognitive distortions, thought form variants, and sensory perceptual experiences comprising psychosis are viewed as a natural propensity derived from the evolution of human intelligence. To facilitate reality congruency typically necessary for adaptive functioning cognitive regulatory control processes normally prevent these extreme forms from entering the conscious and awake state. During sleep when there is no need for reality congruency the cognitive regulatory control processes are deactivated and psychotic equivalents are expressed. The negative symptoms of schizophrenia are seen as arising from diverse neural damage that also impairs to varying degrees the cognitive regulatory control processes, thus producing psychosis. The pattern of neural damage determines the negative symptom profile, and the impact on cognitive regulatory control processes influences whether negative or positive symptoms dominate or exist in relatively equal proportions.

Even though psychosis largely arises due to damaged or impaired cognitive regulatory control processes, it can also serve a defensive function as evident in hallucinations during grieving reactions, and delusions in delusional disorder and paranoid personality disorder. To facilitate defensive functioning cogni-

tive regulatory control processes can be temporarily deactivated, as occurs during sleep. Both defensive deactivation and damage/impairment likely operate on a spectrum with schizophrenia representing minimal defensive deactivation and maximal damage/impairment, and hallucinations during grieving the reverse. Conditions such as delusional disorder and paranoid personality disorder involve both mechanisms. Ultimately, the key to psychosis is then the cognitive regulatory control processes that when damaged or impaired result in psychotic illness, and when deactivated allow psychotic equivalents during sleep or psychotic defenses when awake and conscious.

Conflict of interest

None declared.

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