

Moral emotions and auditory verbal hallucinations in schizophrenia

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Adolescence and early adulthood are characterized by the development of cognitive and social skills necessary for autonomous functioning in adult roles. As classically described by Erik Erikson, this developmental process involves forging a meaningful sense of identity, comprising a worldview, set of moral values, and occupational aspirations. This may require individuals questioning or defying the expectations and norms they have learned within the social context of their upbringing; simultaneously they remain acutely sensitive to the judgment of their peers. This developmental period encompasses the age range in which schizophrenia and other psychotic illnesses are most likely to present. As early as 1914 Sigmund Freud postulated a connection between auditory hallucinations and the formation of an independent moral perspective, which served as the basis for his concept of the superego. However, the connection between processes of identity formation and development of psychosis has not been extensively investigated with the current technologies and knowledge base of biological psychiatry, possibly due to the challenges inherent in operationalizing and measuring aspects of personal and moral identity. In this theoretical review we aim to identify areas of overlap between normative developmental processes in the transition to adulthood, the experience of moral emotions, and the phenomenology of hallucinations in schizophrenia, to build a conceptual framework for novel approaches to the study of psychosis.

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INTRODUCTION

Hallucinations and delusions are cardinal symptoms of schizophrenia and related psychotic disorders. These experiences are often not recognized by patients themselves as symptoms of mental illness, but instead are perceived as real. To others, these symptoms appear to represent a startling loss of touch with reality. However, hallucinations and other unusual perceptual experiences are not uncommonly experienced by people without any psychiatric illness. Children, in particular, may experience hallucination-like experiences that resolve without progressing to a psychotic disorder as they mature^{1,2}. The distinction between delusions, over-valued ideas, and unusual beliefs is often difficult to establish without close attention to social context. Clinical phenomenology thus does not allow a full understanding of these experiences unless it is placed in the context of normative cognitive and social development.

In previous work we attempted to re-assess delusion formation by placing it within the framework of ontological development³. This theoretical framework is based on the concept of social construction of reality, in which we assume that no individual person can have a comprehensive and completely accurate understanding of 'objective' reality. Instead, individuals develop their own unique understanding of the world, for which we use the term 'ontology.' An individual's ontology is based partly on direct experience but also on learning collectively accepted ideas, for which we use the term 'consensus reality' regardless of whether this knowledge is more specifically understood as religious, scientific, or cultural. We argue that the transition to adulthood is a developmental period in which 'ontological adaptation' features prominently; by this we mean that adolescents begin to critically and autonomously re-assess what they

have been taught, seek to learn and experience new things, and otherwise prepare for adult roles by honing their understanding of personal identity, moral values, social roles, and corresponding knowledge or belief systems. For some people this process may be relatively uncomplicated, as they largely adopt and conform to prevailing consensus reality⁴. For others, this process involves challenging and defying social conventions. Among the considerable heterogeneity of this form of development, we argue that a greater tendency to interrogate and challenge the learned norms of childhood, though still within the bounds of normative development, represents a risk platform for psychopathology, including psychotic experiences.

This developmental process has been previously studied in terms of political and religious socialization in transition to adulthood. Twin studies suggest that both political and religious attitudes are driven by environmental factors (especially parental and peer influences) in adolescence, but in early adulthood genetic influence becomes more influential, especially in individuals who leave their parents' home^{5,6}. Parental religiosity is a primary predictor of children's religiosity, especially when family life is harmonious and supportive⁷. From early adolescence into early adulthood, about 48% of youths remain stable in their religious identity, with smaller proportions either changing religion or becoming nonreligious⁸. Individuals who report increasing doubt about religious beliefs across this time period tend to show higher levels of depression compared to individuals with more stable religious beliefs⁹. Surprisingly both increases and decreases in religiosity from childhood to adulthood may be associated with higher risk for substance use disorders, compared to people with stable religiosity¹⁰. The personality trait of openness to experience, which encompasses curiosity and interest

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in novel ideas, is associated with decreases in religiosity over time – though this effect was only found in areas in which religion is more culturally prominent^{11,12}. Thus, although individual trajectories in religious identity vary considerably, on a population level the data suggest that stability in religious identity in the transition to adulthood is common and associated with more favorable mental health outcomes¹³. In contrast, individuals who question the beliefs they grew up with and are motivated to explore alternatives may face greater mental health challenges in transition to adulthood; this may be a necessary trade-off for greater intellectual achievement and non-conformist principles^{14,15}.

In our previous articulation of these ideas we focused on developmental processes relevant to delusion formation, though we must note that this theoretical framework is not entirely original; other recent publications have provided complementary perspectives on delusion formation that similarly emphasize the crucial role of individuals' attempts to establish personal meaning in their experiences^{16,17}. Here we attempt to extend this framework to improve our understanding of auditory verbal hallucinations (AVH). Individuals with psychotic disorders do not always experience both delusions and hallucinations, but the co-occurrence is frequent enough that, employing Occam's razor, a theory explaining the origins of one experience must also contribute to understanding the origin of the other. To accomplish this, we revisit processes of ontological development, with a focus on how individuals monitor their own behavior in regard to social norms and the relationship between this self-monitoring and the phenomenology of AVH.

SUPEREGO, THE INTERNALIZED OTHER, SOCIAL AGENT REPRESENTATION: THE SOCIAL CORE OF ONTOLOGICAL DEVELOPMENT

As youths begin to develop an individual understanding of the world, they retain and continue to develop a parallel understanding of consensus reality. As in the theory of mind, social activity depends in part on being able to understand what other people understand to be true and important¹⁸. The worldview of important people in an individual's developmental environment (parents, teachers, religious figures, etc) retains some influence as a 'default' perspective on moral rectitude. As young people begin to develop their own personal sense of ethics and justice, they are likely to be confronted with unique experiences that they have not had time to assess within their own evolving individual perspective. In these cases, they are likely to fall back on lessons, stories and platitudes learned in the past to at least gauge how a 'typical' person would act in that situation. As their individual ontology becomes more distinct from consensus reality, the latter becomes associated with 'others' in contradistinction to the 'self'. This is essentially the same concept that Freud advanced with the term 'superego,' as a part of an individual's psychic structure that is often perceived as an external force. Interestingly, Freud began his conceptualization of the superego by observing people with psychotic symptoms – "It would not surprise us if we were to find a special psychical agency which performs the task of seeing that... the ego ideal is ensured and which, with this end in view, constantly watches the actual ego and measures it by that ideal. Patients... complain that all their thoughts are known and their actions watched and supervised; they are informed of the functioning of this agency by voices which characteristically speak to them in the third person... This complaint is justified; it describes the truth. A power of this kind, watching, discovering and criticizing all our intentions, does really exist. Indeed, it exists in every one of us in normal life" (Ref.¹⁹, pg. 95).

To be clear that we are not attempting to comment on the psychoanalytic literature regarding this concept we will use the term 'internalized other' as opposed to 'superego' to refer to this

enduring perception of consensus belief. Furthermore, we will refrain from referring to this construct as a 'conscience'; this term is best reserved for the moral aspects of an individual's ontological development and deeply enmeshed with their sense of personal identity. The internalized other can provide a similar function as a conscience: providing a sense of what is right or wrong in a given situation and providing 'feedback' regarding one's current behavior. However, the internalized other and conscience may provide opposing judgments (for example, a person may have been taught as a child that homosexuality is sinful, but may come to personally disavow this belief and befriend a gay peer), and this discord can produce the deep anxiety of being wrong, even when an individual is doing precisely what they feel is truly right and just. This is in line with the self-discrepancy theory of Higgins, which distinguishes between 'actual self' self-representation (who an individual feels that they really are) and the 'ideal self' or 'ought self', which are guides for personal aspirations and external influences on development, respectively²⁰. For the purposes of this manuscript, we see the 'ideal self' as roughly analogous to moral conscience, and the 'ought self' as analogous to the internalized other.

Higgins' theory suggests that differences between these self-representations can lead to psychological distress²¹. Further research has suggested a non-specific relationship between self-discrepancies and negative emotions, including symptoms of anxiety, depression and paranoia^{22–24}. One recent study employed a self-discrepancy approach to participants with psychosis with the added element of measuring the difference between self-representations and how the voices of people with AVH described them; they found fair correspondence between voice content and the extent of difference between actual and ideal/ought self-representations, supporting the concept that voices could be rooted in self-regulatory psychological processes²⁵.

Inherent in the concept of internalized other is the sense of 'otherness'. Ordinarily people can remain aware that this 'other' is still a component of their own mind – a private audience that the individual can use for rehearsal before performance in real life²⁶. 'Felt presence,' the sensation that another person is present when a person is alone, may be an experience intermediate between a consciously imagined audience and hallucinatory experience; people prone to experiencing AVH are also more likely to experience 'felt presence'²⁷. Otherness is central to the phenomenology of AVH.

PHENOMENOLOGY OF VOICE-HEARING

Dopaminergic innervation of the prefrontal cortex and increased density of dopaminergic receptors are notable features of normative brain development in adolescence and are crucial for driving novelty-seeking and experience-dependent plasticity²⁸. The link between neurobiological development and phenomenology of psychosis has been previously made in the "aberrant salience" model. Broadly this model posits that abnormal dopaminergic signaling disrupts the process by which 'importance' is assigned to stimuli and ideas, leading the patient to struggle with comprehending a world in which their attention is captured by seemingly irrelevant items; this model is backed by evidence of increased dopamine synthesis and release in schizophrenia, and clinical findings that D2 antagonists work by "dampening" salience²⁹. Here we extend this theory by suggesting that heightened salience may be assigned to conflicts between the internalized other and conscience. For example, one may experience a dilemma where one's conscience holds a certain moral inclination, whereas the internalized other rules this inclination as unsanctionable. This conflict may enhance the salience of the internalized other, as well as associated distress, preventing a balanced resolution of the moral conflict. In the cases of people with schizophrenia that hear voices, insight into the

internal origin of this phenomenon may be lost. This may be due to a variety of factors including the internalized other gaining exaggerated importance in this state and a growing sense of alienation or 'otherness' of the internalized other (relative to conscience). Thus, the individual may end up hearing voices that are critical towards oneself – one of the most common types of auditory hallucinations.

Surveys of phenomenology in people with psychosis indicate that a considerable portion of people who experience AVH endorse feeling that their hallucinations act in part as a form of conscience or help guide them navigate dilemmas; the voices are often critical, insulting, or "bossy," though are sometimes helpful; the voices not uncommonly can be identified with characteristics related to what people have experienced in their past; and there is often a sort of intimacy in that the voices seem familiar with the individual^{30–32}. Another phenomenon consistent with AVH being rooted in the internalized other is the experience of hearing voices in people with schizophrenia who have been deaf since birth or early development³³. This limits any interpretation of AVH as originating in aberrant perceptual processes but is consistent with AVH as messages received from an internalized understanding of what others might think.

Current neurocognitive theories on AVH include inner speech models, which posit that AVH results from misinterpretation of normal inner speech as being external in origin, and memory-based models, in which AVH stem from failure to inhibit the intrusion of latent thoughts and memories into consciousness^{34,35}. Neurocomputational theory suggests a predictive coding model that could apply to both delusions and hallucinations, in which a neurobiological mismatch between expectations about the environment and actual stimuli results in aberrant perceptions and impaired incorporation of meaningful feedback about reality³⁶. Although a thorough review and critique of these theories is beyond the scope of the current manuscript, there are several ways in which the concept of the internalized other can be useful in integrating these theories with phenomenological evidence.

A primary challenge for these theories is to explain why *auditory* verbal hallucinations are by far the most prominent form of hallucinatory experience in schizophrenia. The inner speech theory is intuitively appealing as it provides an explanation of why hallucinations in schizophrenia most frequently take the form of AVH in a way that accounts for normative cognitive processes. Surveys of people who experience AVH indicate that for a substantial portion, the AVH are not experienced specifically as auditory but may have more of a "thought-like" aspect³¹. Individuals with psychotic disorders and experiencing AVH report higher levels of dialogic and evaluative/motivational inner speech than non-clinical controls, and greater experience of these components of inner speech was associated with greater severity of AVH³⁷. The increased evaluative/motivational inner speech could reflect internalized stigma or low self-esteem³⁷ but may be further indication that the border between inner speech and AVH is fuzziest when it comes to matters of determining what is 'right' and 'wrong,' that is, the function of the internalized other.

A second challenge for theories on hearing voices is explaining the social aspects of the experience; AVH are frequently experienced as having distinct and often stable identities³⁸. Inner speech models can explain why hallucinations take the form of voices but not necessarily why they are perceived as distinctly other; memory-based models provide an understanding of some instances of AVH, such as those related to traumatic experiences, but cannot account for the wide variety of AVH; and prediction error models have not attempted to explain the social nature of AVH³⁹. Inner speech can take the form of dialogue with the internalized other, with the latter rooted in formative experiences with significant others in one's developmental history. Even if the

internalized other is not experienced as a distinct inner voice, it is experienced as if it were a social entity.

A third challenge for theories on AVH is to explain why the voices are most frequently experienced as being hostile, insulting, and commanding. Traumatic experiences and heightened monitoring of threats provide partial explanations, but a more complete explanation may involve a self-monitoring process⁴⁰. The internalized other serves this self-monitoring function as an inherently judgmental alert to failures to meet moral standards; this also helps to explain why AVH are intrusive, compelling, and/or meaningful.

MORAL EMOTIONS AND AUDITORY VERBAL HALLUCINATIONS

As in the parallel theories of Freud and Higgins, the 'internalized other' monitors gaps between what is extant and what is ideal. If this concept is valid, the appearance and function of the internalized other, or the distress from incongruence between actual and ought self-representation, should be most evident in situations involving deviance from social norms. Hence, we must consider how AVH are related to the typical emotional and cognitive responses to recognition of violations of how things should be: anger, disgust, shame and guilt, collectively described as "moral emotions"⁴¹. Attention to violation of norms is deeply rooted in our experience of the world. Young children exhibit limitations in reasoning about possibilities, such that they have trouble distinguishing what is morally unacceptable from what is unconventional, in a similar way that they have trouble distinguishing the likelihood of physically impossible versus physically unlikely events⁴². Children tend to disapprove of individuals who do not conform to expectations of the group or category the individual belongs to⁴³. People eventually develop more advanced moral reasoning that can account for contextual factors and ambiguities, but even adults are prone to cognitive biases in which immoral or irrational possibilities are discounted in pre-reflective processing⁴⁴, and people are seen as 'deserving' of their fate, whether positive or negative⁴⁵. Similarly, Theriault and colleagues have argued people are biased towards conforming to social expectations due to a "sense of should," referring to an emergent psychobiological phenomenon that incorporates social norms and situational factors into a predictive coding function⁴⁶.

People with schizophrenia tend to experience negative emotions more frequently in everyday life compared to people without a psychiatric diagnosis; prominent among these negative emotions are anger and disgust^{47,48}. Qualitative assessment of the content of AVH suggest that for a majority of people who experience them anger, shame, and guilt are prominent underlying themes⁴⁹. Shame is a universal feeling of recognizing a flaw or failure within ourselves. Theoretically this can be considered an adaptive capacity, as shame provides a signal and motivation for individuals to seek to avoid punishment or conflict in situations where the individual may have been judged by others to be wrong⁵⁰. Shame may mediate the relationship between traumatic experiences and hallucination-proneness⁵¹. In another study of people with schizophrenia, experience of shame mediated the relationship between unusual perceptual experiences and delusional ideation⁵². In a similar vein, AVH with a theme of guilt "... can be related to an internalized voice of moral authority that can guide interpersonal behavior enhancing social relationships..." (50, pg 6).

Common reactions to the perception that "I should have acted that way, but I acted this way" are feelings of anger, guilt or shame. Perceptions that "(another) person should have acted that way, but they instead acted this way" similarly incite moral emotions such as anger or resentment. There is likely considerable between-individual variability in terms of sensitivity to perception of norm violations as well as the intensity of emotional and cognitive responses to these violations. There are existing

methods to measure these tendencies that can be used to test the hypotheses underlying the current theoretical framework. For instance, a self-report questionnaire, the Justice Sensitivity Inventory (JSI), measures the degree to which people react negatively to the perception of injustice, whether committed against oneself, against another person, or whether one is responsible for inflicting injustice on another⁵³. Higher scores on the JSI are associated with increased experience of depression, anxiety, self-injurious behavior and substance use^{54,55}. There are multiple behavioral tasks that measure cognitive biases related to norm violations, which can be combined with functional MRI to probe the neural circuitry of moral perception.

EVIDENCE FROM FUNCTIONAL IMAGING

The particular attention or salience that an individual gives to their flaws and mistakes may predispose them to the experience of hearing voices, and/or promote the specifically negative and hostile nature of the voices^{40,56}. This process of monitoring our internal and external environment and directing our attention to the most salient events is governed by the activity of a functional brain network aptly termed the *salience network* (SN).

The anterior insula is a key hub of the SN, as this region is reliably activated in conditions in which an outcome is different than expected, broadly interpreted as a prediction error signal⁵⁷. This region is also reliably activated during experience of moral emotions, as meta-analyses of fMRI studies have found for shame, embarrassment, guilt⁵⁸, anger⁵⁹, and disgust⁶⁰. More generically, the insula is a key region activated in detection of norm violations⁶¹. This activation of the insula and other parts of the SN is likely homologous to their role in prediction error, but instead of signaling novelty or changes in reward value of motivation-relevant stimuli, may be a signal of 'moral error' to other neural networks. From a phenomenological perspective this function of the SN may be associated with the experience of *something being wrong*, or in the related theory of Therault and colleagues, a violation of the *sense of should*⁴⁶. Since the SN is known to track, monitor and flag discrepancies from what is expected, it may also play a role in monitoring and flagging discrepancies between one's perceptions of "who I am" (or "how I acted") vs. "who I ought to be" (or "how I should have acted"). Moreover, as discussed above, adolescence is a time where many teenagers choose to challenge the *status quo* beliefs of family and community. The SN's job is specifically to monitor and detect deviations from the *status quo*. Consistent with this view, there are several studies suggesting activation of the SN in moral judgment. In one study⁶² participants were asked to complete sentences with a semantically appropriate choice. These choices contained either moral, immoral, or neutral actions in hypothetical scenarios. When presented with either moral or immoral choices, elements of both the SN and the default mode network (DMN) were more activated in comparison to neutral choices. However, in the comparison of immoral vs. moral choices, the two major hubs of the SN – the anterior insula and dorsal anterior cingulate – were more prominently active during immoral choices. In another study, moral reasoning was associated with activation of the SN influencing downstream activity of the DMN; this influence of SN hubs was reduced in patients with frontotemporal dementia, who exhibited less moral constraint in terms of violating the rights of others in hypothetical scenarios⁶³. Finally, a meta-analysis of functional imaging studies involving moral decision-making or moral emotion tasks reported that the major regions involved were key hubs of the SN and the DMN⁶⁴. In schizophrenia, altered functional connectivity between the SN and other networks – in particular the DMN and Central Executive Network – has been found in several studies^{65–67}. Functional imaging studies that have attempted to locate regions of unusual activation in patients with frequent AVH have yielded mixed results, but the most consistent

finding has been increased activity of the left inferior parietal lobule and insula; structural findings also suggest decreased volume of the left insula in patients who experience AVH⁶⁸.

It has recently been theorized that the SN plays a critical role in selecting mental representations for conscious awareness⁶⁹. Since it is clear from phenomenological investigations that AVH are not simply "noise" resulting from ineffective filtering of extraneous stimuli or stochastic activation of latent memories, a more compelling hypothesis is needed. Consistent with Hare's theory, we hypothesize that AVH in schizophrenia may frequently stem from abnormally strong selection of mental representations of moral judgment and norm violation by the SN for conscious awareness. The dysconnectivity between the SN and other functional networks may lead to this 'moral error signal', already associated with the internalized other, being perceived as external in origin. Advantages of this hypothesized model include providing a framework for understanding *what* and *how* mental content gets selected for conscious awareness in the case of AVH, which was previously identified as a limitation of neurocognitive models of AVH⁶⁹.

CLINICAL IMPLICATIONS, LIMITATIONS, AND FUTURE DIRECTIONS

The current theoretical framework presents new possibilities in understanding mechanistically how stressful life experiences may contribute to risk of psychopathology. Some risk factors for schizophrenia such as childhood trauma and bullying represent violations of expectations about how things should be, and other risk factors such as migration and urbanicity may contribute to increased chance of encountering substantial challenges to the moral world learned in childhood. We would thus expect people who experience these to learn that violations of social and moral norms *can* and *will* happen, which in turn may predispose individuals to reject elements of consensus reality, and/or to prefer unique constructions of reality⁷⁰.

Recognition of the role of moral emotions in experience of AVH may be important for understanding suicidality and violence committed by people with psychotic disorders. Feelings of guilt may be particularly associated with suicidal thoughts and attempts^{71,72}. Though people with schizophrenia are more likely to be victims than perpetrators of violent acts, violence driven by psychotic symptoms can be dramatic and unpredictable⁷³. Violent acts committed by patients with schizophrenia may have less to do with the overall severity of their psychotic symptoms, and more with the degree to which delusions and AVH cause them to feel that violence is morally justified and/or necessary⁷⁴. Greater sensitivity of clinicians and family members to perceptions of justice and moral norms in patients' experiences may help with identifying, reframing, and redirecting the intense emotions that may precede self-harm or violence towards others.

The present theoretical framework may also contribute to individual psychotherapy and psychoeducation with patients with psychotic illnesses. Discussing AVH as a manifestation of the 'internalized other' could be a tactic that builds trust and opens new avenues for therapy by acknowledging the inherent meaningfulness of the experience without validating the negative and potentially harmful content of AVH. This may be especially true for the substantial minority of people with psychosis who experience AVH as sometimes being positive or helpful^{31,32}. By minimizing the potentially stigmatizing elements of how psychosis is described, clinicians may be able to improve patient engagement in treatment.

The connection between self-monitoring for norm violations and experience of AVH was made by Freud and later echoed by Nayani and David, who reported that 46% of the participants in their survey endorsed feeling that "their hallucinations had come to replace their 'voice of conscience'" (30, p. 184), as well as by Volpato and colleagues as noted above⁵⁰. However, this idea has not been tested empirically to date. Future studies should consider

incorporating measures of self-discrepancy and justice sensitivity, as well as more probes regarding moral themes in phenomenological assessments of AVH. Crucial to the clinical value of the theory is the understandability and acceptability of focusing on moral emotions to patients and their providers. To this end, a qualitative survey of people with lived experience of psychosis regarding their impressions of varying theoretical models of AVH, similar to what has recently been done for conceptions of identity disturbance in psychosis⁷⁵, would be informative. We have argued that abnormal salience of moral violations contributes to the experience of AVH. This hypothesis could be tested on the psychopharmacological level, as dopaminergic agents have been found to influence behavior and perceptions of fairness in neuroeconomic games^{76,77}. Further paradigms could be developed to test dopaminergic manipulations on detection and intensity of emotional reactions in response to moral violations. Such paradigms could also be adapted for functional neuroimaging to test the hypothesis that abnormal functional connectivity of the insula is associated with severity of AVH. Even if this course of research provides support for the proposed framework, we should anticipate that the model would not account for the full variety of hallucinatory experiences in psychotic disorders, given their broad heterogeneity. In particular, non-verbal auditory, visual, and olfactory hallucinations may not be easily understood within the framework of moral perception.

A final cautionary note for the development of research on this topic is the unresolved debate over the definition and nature of morality. Cross-cultural evidence indicates that some behaviors, mainly related to cooperation, are universally regarded as moral⁷⁸. This supports the concept of a specific psychological function for assessing morality, as articulated in Social Domain Theory; however, the scope of behaviors recognized as moral/immoral, and the distinction between norms that are specifically moral versus conventional in nature, remain contentious⁷⁹. Limited evidence from imaging studies indicates that there are both common and dissociable brain regions activated when people rate the wrongness of moral versus conventional norm violations⁸⁰. Further complications are likely when applying these theories to patients with psychotic disorders; although people generally consider moral violations as more wrong than violations of conventional norms, this difference is reduced in schizophrenia⁸¹.

CONCLUSIONS

We propose that the content of some auditory hallucinations in schizophrenia stems from abnormally strong entry of mental representations of moral judgment into conscious awareness. These mental representations are built through social development as a tool for determining how one's actions will be judged by others, and hence even in normal development are perceived as inherently related to important others in one's life. In psychopathology, this perception of moral judgment as being related to others can be amplified to the point where it is perceived as being external, and contributes to intense experience of moral emotions. This amplification may be driven by stress, uncertainty, and prior experience of harsh criticism, bullying or abuse. These experiences are prominent in the period of transition to adulthood when individuals increasingly confront novel situations requiring them to think and act independently. This model aims to provide a framework for combining developmental psychology with clinical phenomenology and neuroscience to generate new directions in understanding psychosis. If validated, this model also offers a way of discussing symptoms with patients and families that minimizes stigma and facilitates trust.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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