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The Specificity of Paranoia and Uncertainty

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Paranoia is associated with significant suffering and additional challenges in caring for oneself, such as social isolation, suicidality, and poor treatment compliance. For individuals experiencing paranoia, defined as a belief that others are intentionally trying to harm the individual, the symptoms can range from limited social interaction with peers to verbally or physically lashing out at loved ones or strangers. Previous work has suggested that paranoia lies on a continuum (1). When examining clinical levels of paranoia, much of the literature focuses on diagnostic groups, such as schizophrenia spectrum disorders. Yet for disorders that include psychosis, which can be quite heterogeneous, a focus on problematic symptoms may offer more targeted treatment. There has been increasing interest in paranoia, which is responsible for approximately 70% of delusions and therefore may provide the most leverage to address where these delusions come from and how they are maintained.

An important aspect of symptom-specific assessment is distinguishing symptoms from one another. Paranoia has overlapping components with worry, such as fixation on unpleasant thoughts and concern about unlikely outcomes. Importantly, previous work has shown that persecutory worry and general worry are related, but separable (2). In addition, it is important to separate paranoia from other delusional content (grandiosity, somatic, erotomania, etc.). This may begin to answer how delusions arise: Is everyone who experiences a delusion simply susceptible to cognitive distortions that exaggerate issues in their lives? Or do delusions arise through multiple methods?

In the current issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, Sheffield *et al.* (3) developed a study that focused on paranoia and its relationship to belief updating and worry. They recruited 45 individuals with schizophrenia, a group that more commonly experiences paranoia, and asked them to complete a 3-option probabilistic reversal learning task. They also recruited 46 individuals with no psychiatric diagnoses as healthy control subjects. Participants were given the choice between 3 decks of cards that rewarded the participant 90%, 50%, and 10% of the time, respectively, and gave all participants a chance to learn which deck was the best. However, once the participant demonstrated that they had learned the best deck (getting 9 out of 10 correct), the best deck switched, constituting a reversal. The authors included a change in the contingency of rewards without informing the participants; these components of the paradigm ensured that there was sufficient uncertainty about whether a particular loss was due to noise or due to a true change in the environment. This focus on uncertainty was important in assessing individuals' beliefs about changes (i.e., volatility) in the environment.

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Behaviorally, individuals with schizophrenia responded in a more erratic manner than healthy control subjects. Most strikingly, these participants were more likely to switch after being rewarded (referred to as the win-switch rate), making it more difficult to consistently win on the best deck and achieve more reversals. While not discussed in this study, previous results have shown that this leads to overall lower earnings (4), negatively impacting participants. Furthermore, win-switch rates were significantly correlated with paranoia, consistent with previous findings, showing that this unconstructive behavior may be associated with paranoia specifically.

To extract and quantify individual beliefs about the noisy environment, the researchers applied a Hierarchical Gaussian Filter, which estimated initial beliefs about volatility in the task (μ^0_3) and sensitivity to volatility (κ). Here, volatility references the amount of change and instability within the task environment. They found that interview-rated paranoia was significantly associated with μ^0_3, suggesting that paranoia is associated with a greater belief that the environment is unstable. Individuals with elevated paranoia had higher κ compared with individuals with low paranoia, suggesting an increased sensitivity to volatility in the environment. These computational measures show that paranoia is associated with a prior belief that the world is noisy and leads to more uncertainty about causes when interpreting events in the environment.

To further examine the specificity of paranoia, Sheffield *et al.* examined the relationship between these parameters, worry, and unusual thought content. They found that beliefs about task volatility (μ^0_3) were specifically correlated with persecutory worry, but not general worry, social anxiety, or perseverative thinking. Furthermore, paranoia had a significant indirect effect on the relationship between μ^0_3 and overall worry. As the authors suggest, this is a meaningful result associating paranoia with beliefs about the instability of the environment, separating it from other forms of worry. Importantly, they also dissociated μ^0_3 from unusual thought content, making this result appear more related to paranoia and not to a general increase in cognitive distortions. However, there are still several open questions.

First, while hypotheses focused on the role of worry in maintaining paranoia, there is still an open question about the causal relationship (if any) between these belief priors and paranoia. The results from this study identify a maintenance factor: It is difficult to adjust beliefs with new information because it is unclear what is true and what is noise. But do these beliefs about volatility exist prior to paranoia that may lead to greater susceptibility to a stressor, consistent with the stress-vulnerability diathesis hypothesis (5)? A person may also develop paranoia related to other events (again, stressors and genetic risk) and over time learn to expect greater uncertainty in the world. Finally, a third factor may affect both parameters. One study has identified that environmental changes can affect the relationship between paranoia and prior beliefs about volatility: As the pandemic progressed, individuals became more paranoid, had higher win-switch rates, and increased prior beliefs about volatility, but this also interacted with the level of proactive pandemic response from their state (6). Separate work will be needed to identify a causal relationship between paranoia and belief updating.

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Second, previous studies using this method argued that given the nonsocial aspect of the task, paranoia may not be related to social functioning but rather to a more general cognitive disposition that applies to social situations. However, other studies have shown paranoia specifically related to social interactions (7,8). Barnby *et al.* (7) used the same task as Sheffield *et al.* (3) as a control task to compare with a similarly structured dictator game, in which participants were told that a partner chose how to divide a sum of money between the partner and participant; participants learned that one partner was fair and one was not, which reversed halfway. Here, individuals could also decide if they believed the choices were associated with either self-interest or harmful intent. Using a Bayesian belief model, Barnby *et al.* (7) found that paranoia was associated with uncertainty in the partner's beliefs and greater rigidity in applying harmful intent (but not self-interest) to the partner. These results were consistent with those of Sheffield *et al.*, showing greater noisiness in choices and poor identification of the optimal deck associated with paranoia. They concluded that while individuals had greater uncertainty about the world and increased difficulty updating beliefs, higher paranoia was related to beliefs of harmful intent from their partners (7). In addition, Kazinka *et al.* (8) created a model specific to social decision making based on the Fehr-Schmidt Inequity Aversion Model (9). In this task, players choose whether to trust a partner to share a large amount of money equally or to take an uneven amount in which the player could potentially lose money; critically, in one condition the partner would receive less money to ensure that the player lost money (spite). Kazinka *et al.* identified that beliefs about a partner's willingness to behave spitefully were associated with paranoia. These findings similarly show that prior beliefs affect an individual's choices yet have different specificity to social issues.

Lastly, the study by Sheffield *et al.* (3) focused on individuals with psychosis, as persecutory delusions are more common in this population. Previous results identifying this relationship between paranoia and belief updating in a general population suggest that it may apply more broadly (10). This relationship may not be specific to psychosis but may extend to other psychiatric disorders where paranoia may emerge. For example, paranoia has some association with disorders such as borderline personality disorder and posttraumatic stress disorder and with some forms of dementia, such as Alzheimer's disease. In addition, there may be psychosocial factors, such as experiences of discrimination, that may further influence increased paranoia and uncertainty about the world. Broader research in this area may elucidate the extensibility of this relationship.

The work by Sheffield *et al.* (3) is an important piece of the puzzle as we continue to focus on symptomatology specifically, particularly in disorders that can be quite heterogeneous. These findings provide valuable future directions and support for treatment for paranoid delusions. From this work, there are still questions about the causal relationship between paranoia and beliefs about volatility, the importance of social factors on paranoia, and the extensibility to other disorders. As these questions are examined, the answers will provide more clarity about the treatment and prevention of persecutory ideations.

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