



COVID-19 and Brain Health

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Biotechnology Kiosk, 2, 6 (2020)
DOI: <https://doi.org/10.37756/bk.20.2.6.1>



Global pandemic takes a toll on our brain health: how unexpected uncertainty makes you vulnerable to paranoia

Abstract

Human beings are susceptible to their changing social environments and these changes take a toll on our brain health. In a state of crisis such as the global pandemic Covid-19 we have experienced random unexpected uncertainty which can lead to induced paranoia in healthy individuals. Paranoia is a key symptom of serious mental illness, characterized by the belief that other people have malicious intentions and that harm will occur due to the deliberate actions of others. Although it also exists in normal populations but gets triggered more in cases of stress, social threats, drug abuse and personality disorders. Here we discuss a study which employed computational modeling and reversal learning behavior to estimate belief updating across online participants, individuals with and without mental illness and rats chronically exposed to methamphetamine, an elicitor of paranoia in humans. This study is an attempt to unravel the underlying mechanism of paranoia and give possible cues towards the development of new treatments. If paranoia can be induced in model organisms without taking the social interaction into consideration it will simplify the research intricacies and will open new possibilities of a potential cure.

Keywords: Paranoia; brain health; methamphetamine; reversal learning behavior; Covid-19

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To cite this article: Singh S; Global pandemic takes a toll on our brain health: how unexpected uncertainty makes you vulnerable to paranoia, Biotechnology Kiosk, Vol 2, Issue 6, PP: 4-9 (2020); DOI: <https://doi.org/10.37756/bk.20.2.6.1>

Paranoia: A key symptom of serious mental illness

It is popularly said the biggest fear is *'the fear of the unknown'* and rightly so because what we have not encountered is what we cannot defeat. It is absolutely normal for any human being to harbor fear, anxieties and apprehensions regarding various aspects of life, however, the difficulty arise when we are unable to overcome these dominant negative mental traits. Especially during these difficult times of global pandemic caused by COVID-19, mental health is a matter of current interest and has become a hot-spot issue with everyone around suddenly becoming aware of it. To briefly explain mental health comprises our psychological, emotional, and social well-being. It affects our thoughts, feelings as well as actions. In recent times we see this mental health issue being acknowledged at various social media portals and confessions by celebrities will always add the extra zing to it. However, for anyone who takes interest in the topic will have to turn towards core neuroscience for answers.

All living organisms are constantly evolving and adapting to their changing environments and each one of us has been programmed biologically to respond to these changes. Our survival instincts are strong enough to enable us to fight and face any drastic change in our surroundings. However, for human beings it's not just about survival but also about maintaining sanity and sustaining brain health.

We have highlighted and addressed the importance of brain health and mental wellbeing in two of our previous articles namely *"The tussle between the*

developing adolescent brain and dietary choices: who's the target who's the trigger?" and *"Worries make you look older: unraveling the science that connects stress with graying in human beings."* Delving further in the issue we chose 'paranoia' as our current topic for discussion.

Paranoia is a key symptom of serious mental illness, characterized by the belief that other people have malicious intentions and that harm will occur due to the deliberate actions of others (1). For a layman paranoia can be explained as a thought process that makes you irrationally suspicious and mistrust others. Paranoid individuals feel that someone is out to get them or they're being persecuted. They fear the threat of physical harm even if there is no possible danger. It is a prevalent trait in dementia patients, drug addicts and people with personality disorders. However, paranoid behavior is also observed in perfectly healthy individuals under conditions of stress, competition, drastic changes and so on. A team of researchers from Yale University have provided scientific evidence in favor of a theory that unexpected uncertainty can breed paranoia. Their study highlights the fact that in times of unexpected uncertainty such as a global pandemic like COVID-19 people are likely to get prone to paranoia. In this article we shall briefly describe and discuss this interesting piece of literature published in the journal eLife (2).

What the study unravels?

According to Yale's Philip Corlett, associate professor of psychiatry and senior author of the study, "When our world changes

unexpectedly, we want to blame that volatility on somebody, to make sense of it, and perhaps neutralize it,". The year 2020 has been wreaking havoc globally in the form of the Covid-19 pandemic. This is a changing global scenario where we as a human race stand together against fighting this

catastrophe. In times of unexpected uncertainty our abilities to cope with a crisis are challenged and this leads to mental health problems like paranoia. Figure 1 summarizes the brain areas associated with different brain disorders.

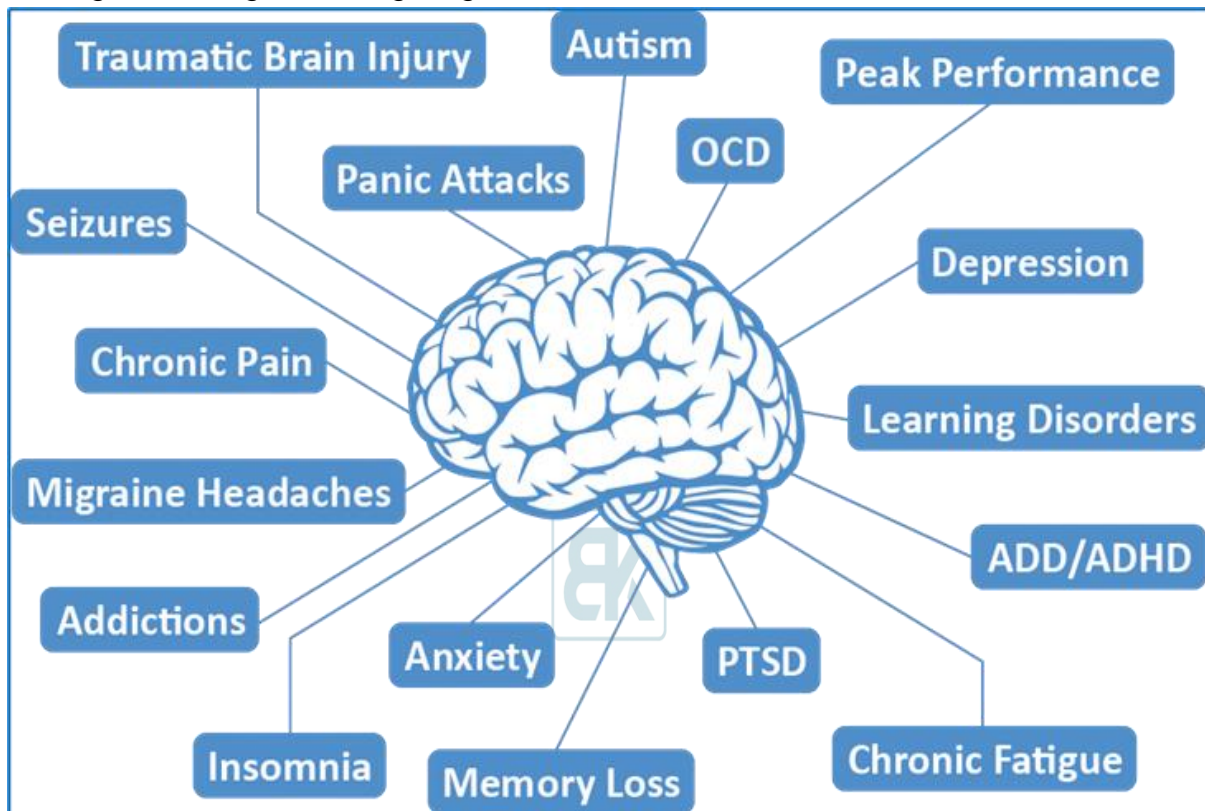


Figure 1: Diagrammatic brain map to show the different areas of the brain responsible for the different brain disorders [Source: <https://www.pngwing.com/en/free-png-pbnom>].

It is theorized that paranoia arises due to an inability to accurately assess social threats. However, lead author of the study Erin Reed and Philip Corlett hypothesized that paranoia is instead rooted in a more basic learning mechanism that is triggered by uncertainty, even in the absence of social threat. According to Reed, "We think of the brain as a prediction machine; unexpected change, whether social or not, may constitute a type of threat -- it limits the brain's ability to make predictions". "Paranoia may be a response to

uncertainty in general, and social interactions can be particularly complex and difficult to predict."

The current study employs the use of reversal learning behavior and computational modeling to estimate belief updating across individuals with and without mental illness and online participants. To briefly explain the study, a series of experiments were carried out where human subjects with different degrees of paranoia were made to play a

card game in which the best choices for success were secretly changed. Individuals with little or no paranoia were slow to assume that the best choice had changed. But paranoid individuals expected even more volatility and unpredictability in the game. Despite winning they changed their choices impulsively and in a more erratic manner. The

researchers then amplified the levels of uncertainty by changing the chances of winning halfway through the game without informing the participants. This sudden unexpected change in the situation made even the low-paranoia participants behave like those with paranoia, learning less from the consequences of their choices.

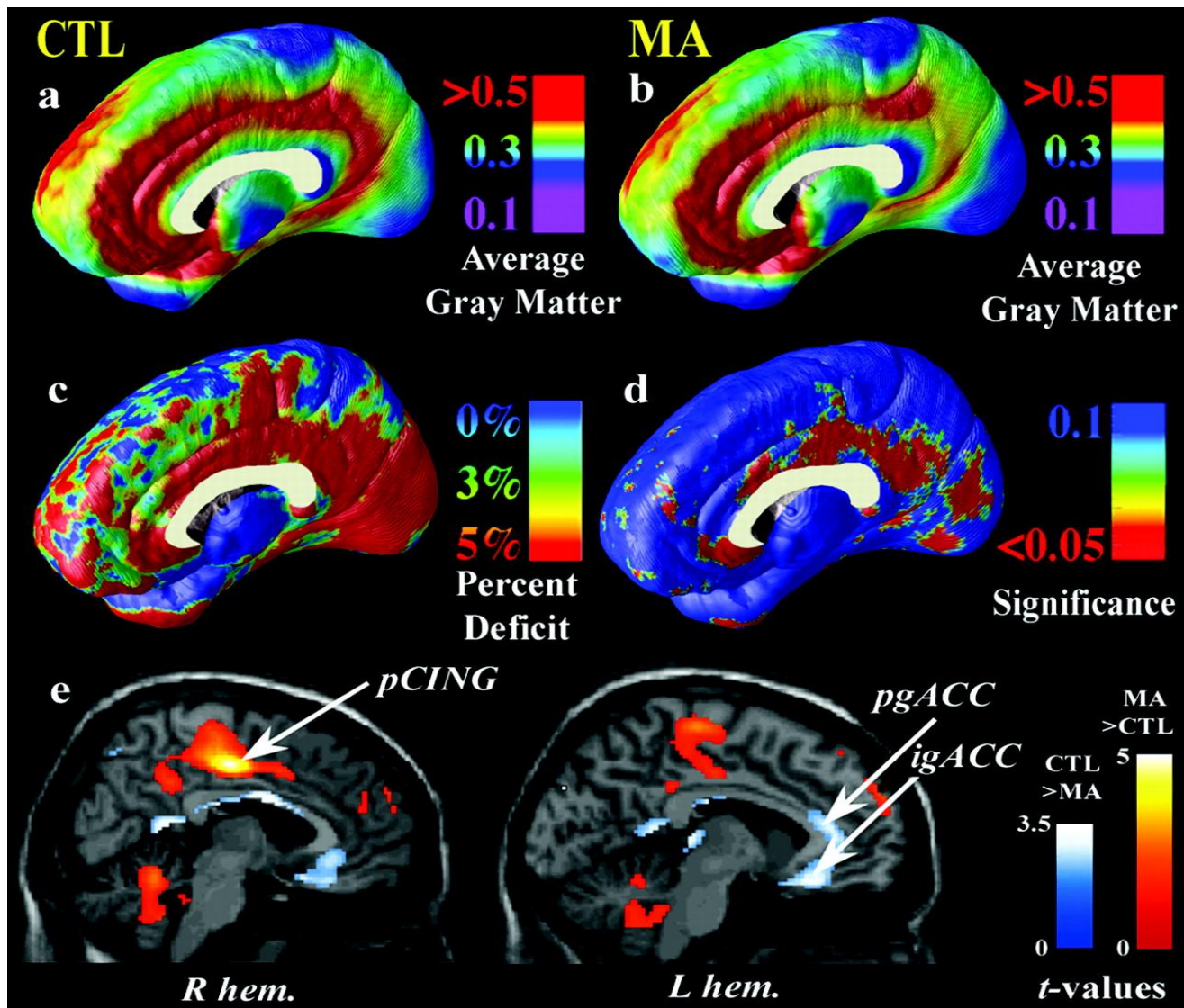


Figure 2: Neuroimaging data of brain of healthy human versus methamphetamine user showing gray-matter differences on the medial brain surfaces. Group difference maps (c) show mean percentage differences in gray-matter volumes between the control group average (a) and the methamphetamine group average (b), according to the color bar. The significance of these reductions is plotted in d as a map of p values [Source: Journal of Neuroscience ,2004(5)].

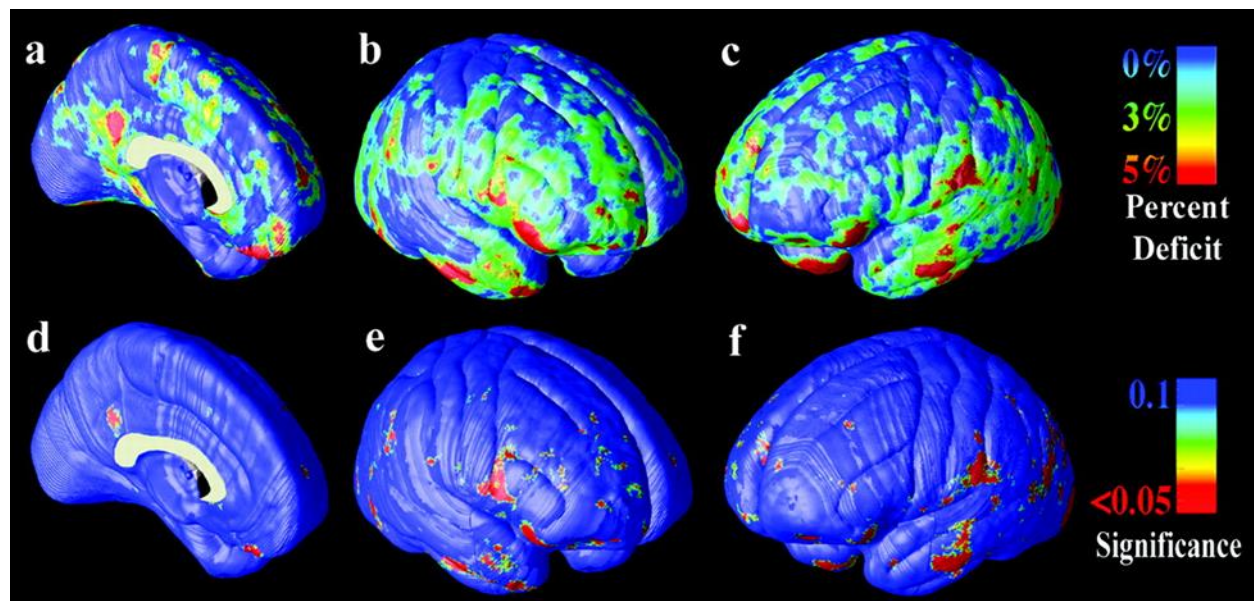


Figure 3: Neuroimaging data of brain of healthy human versus methamphetamine user showing gray-matter differences on the lateral brain surfaces. The mean reduction in gray matter in the MA group, relative to healthy controls, is expressed as a percentage and shown color-coded (red colors-greater reduction; blue colors- no reduction;) [Source: Journal of Neuroscience ,2004 (5)].

In order to check for translation in other species rodent data was also taken into consideration. Yale collaborators Jane Taylor and Stephanie Groman carried out a similar experiment in rats where they trained them to perform a task where best choices of success were changed (3). Rats were chronically exposed to methamphetamine, an elicitor of paranoia in humans. Methamphetamine exposure in rats recapitulates the impaired uncertainty-driven belief updating and rigid anticipation of a volatile environment (2). Therefore, these rats then behaved like paranoid humans and anticipated high volatility and relied more on their expectations than learning from the task. Reed, Corlett and their team then used computational modeling approach and employed hierarchical Gaussian filter (HGF) modeling (4) to compare choices made by

humans and rats while performing these similar tasks. The researchers found that the results from the rats that received methamphetamine resembled those of humans with paranoia. The complexity of the human brain gives rise to a number of brain disorders and anomalies which are sometimes beyond treatment and cure. However, if we can narrow down on the molecular targets and signaling aspects it becomes feasible to design therapy and drugs. This study is an attempt to unravel the underlying mechanism of paranoia and give possible cues towards the development of new treatments. If paranoia can be induced in model organisms without taking the social interaction into consideration it will simplify the research endeavor and will open new possibilities of a potential cure. Figures 2 and 3 show the neuroimaging data of structural

abnormalities in the brains of human subjects who use methamphetamine in comparison to healthy controls (5).

Concluding Remarks

Neurodegenerative diseases and mental health disorders are largely incurable and pose not only a personal health threat but also a social health threat. When a person suffers from a brain disorder or a personality disorder he/she does not suffer alone, instead the entire family suffers. These mental health disorders can go largely unnoticed as people and families often shy away from even acknowledging the root cause of the problem. Therefore, along with medical and scientific research it is equally important that people are sensitized towards these aspects of brain health and encouraged to have a dialogue. Timely diagnosis of a brain disorder is crucial so that it can be managed if not cured. During this time of global crises several nations were under a complete lockdown state. This kind of a sudden uncertainty not only took a toll on our professional and social lives but also affected our brain health. Different people will perceive these changes in different manners; however, getting paranoid in such situations is a common feature. Thus it is important to understand how paranoia can be targeted and treated so that we have better therapeutics to handle brain health during times of global pandemics. The current piece of research has shed light on the various aspects of paranoia in humans as well as the asocial animal species such as rats. Hopefully in near future we shall have better

treatments and therapeutics to cure mental health disorders such as paranoia so that at least we can ensure a population of sane and mentally healthy individuals who can cope with the side effects pandemics like Covid-19.

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