Medical Xpress

Deep brain stimulation study models impulsivity and risk aversion

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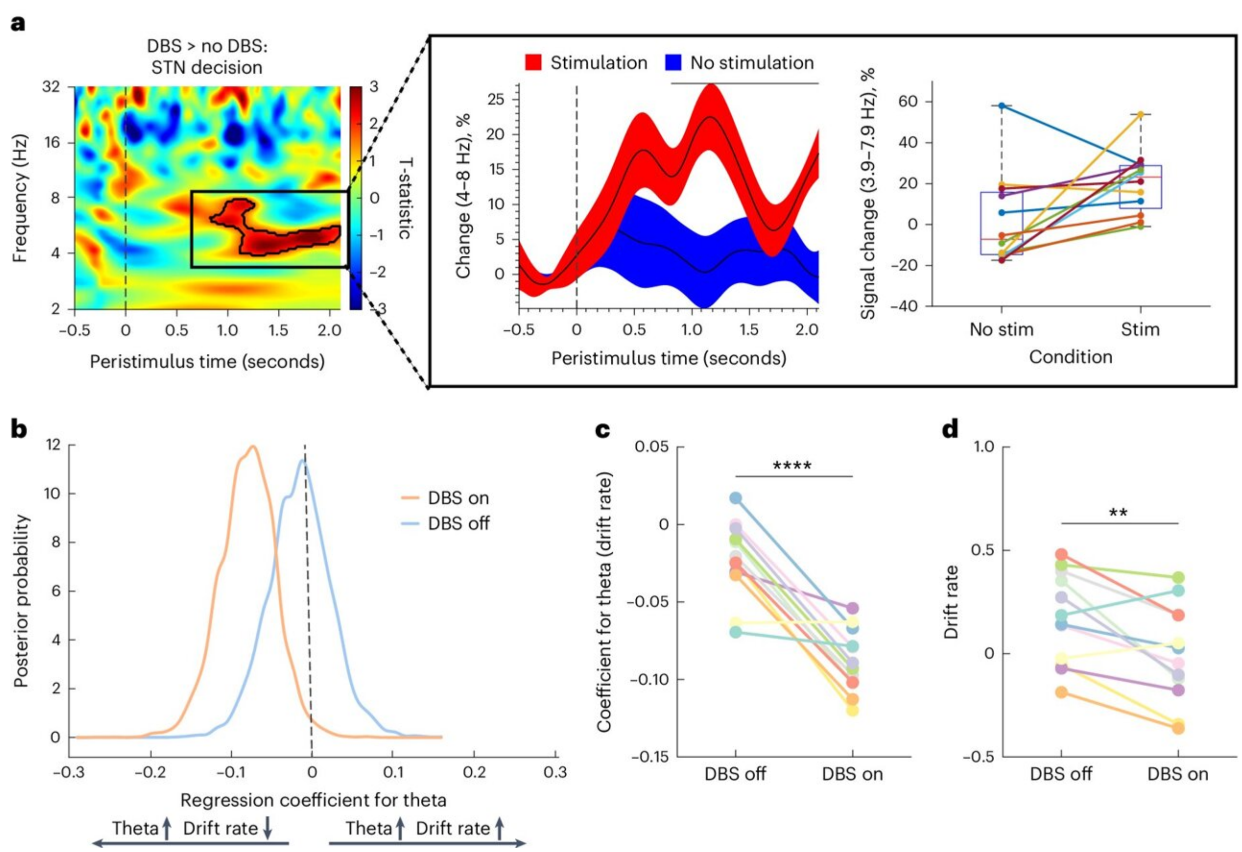


STN local field potential activity following stimulation. Credit: *Nature Mental Health* (2024). DOI: 10.1038/s44220-024-00289-z

Deep brain stimulation (DBS) is a neurosurgical procedure that entails the implantation of electrodes in specific brain regions, to subsequently stimulate these regions via high frequency electric impulses. This procedure is a highly effective therapeutic intervention for various severe neurological and psychiatric disorders, including Parkinson's disease and obsessive-compulsive disorder (OCD).

Researchers at Shanghai Jiao Tong University School of Medicine and University of Cambridge recently used DBS to investigate two opposite behavioral patterns in decision-making, namely impulsivity and risk aversion.

Their paper, published in *Nature Mental Health*, pin-points new objective (i.e., generally applicable to all humans) and subjective (i.e., differing between different individuals) markers of risk-taking.

"Why do we make impulsive decisions that are risky too quickly, disinhibited or choosing immediate gratification?" Valerie Voon, co-author of the paper, told Medical Xpress. "My research group studies impulsivity and how emotions or incentives might influence our decisions, particularly with addictions and compulsivity.

"We are interested in the overlap between illegal (stimulants, heroin), legal (nicotine, alcohol) and behavioral addictions, such as gambling, compulsive sexual behaviors or compulsive behaviors such as OCD."

The key goal of the recent study by Voon and her colleagues was to investigate risk taking, the tendency to make decisions with an expected reward or punishment in situations where outcomes are either easy to predict or hard or impossible to predict. To do this, the team stimulated the subthalamic nucleus (STN) of their study participants using DBS.

"We know that DBS can increase specific forms of impulsivity: what is known as conflict impulsivity, DBS of the STN results in faster choices when choosing between two difficult choices," said Voon.

"This is not always negative and can be functional. For instance, the choices of patients diagnosed with OCD are pathologically slowed. STN DBS can normalize this, so that their choices become faster and closer to those of healthy individuals."

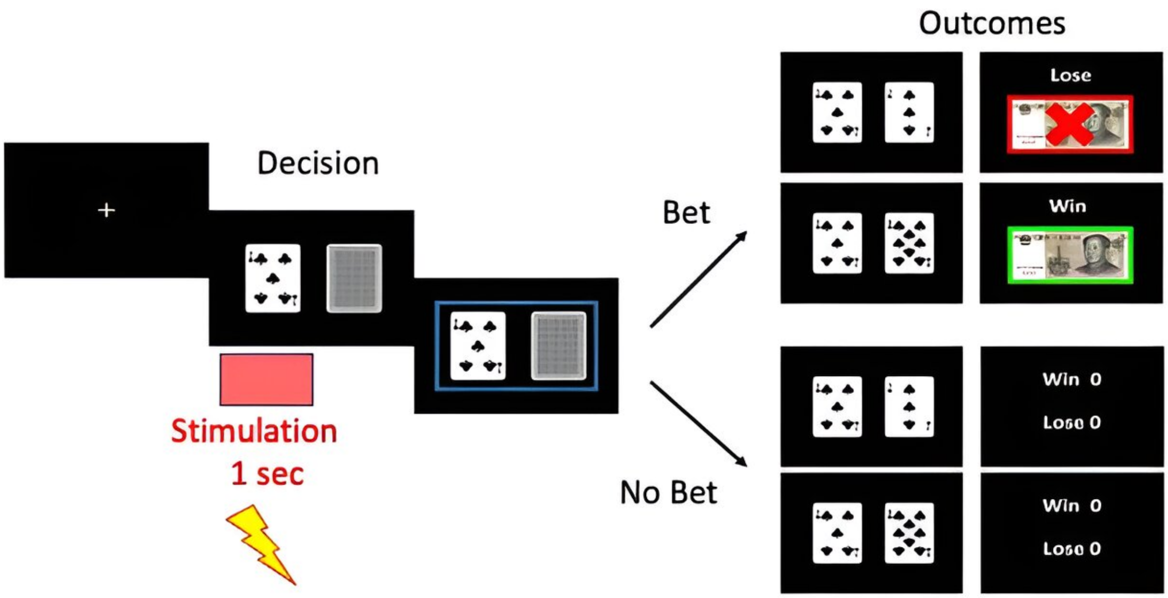
Past studies have found that DBS targeting the STN can also increase risk aversion, thus making individuals more inclined to make safer (i.e., less risky) choices. This means that it simultaneously influences two different dimensions of impulsivity, helping individuals to make difficult decisions faster while also picking the less risky choice.

"The STN is a critical brain region for Parkinson's disease and OCD," Voon explained. "It is the size of a pea and sits within the indirect inhibitory pathway of the frontostriatal circuit. It plays an integrative role in allowing us to calibrate our actions and decisions, by going faster, slowing down or braking our actions, depending on the speed at which we need to make decisions."

Voon and her research group wished to better understand the brain waves underpinning impulsivity during different types of decision-making. Using DBS electrodes implanted into the STN of their participants, they were able to gather new insight about how the brain of different individuals processes different aspects of risky decision-making.

"We also investigated what happens if we stimulate the STN for 1 second, specifically in terms of how this affects risk seeking and the brain waves," said Voon. "This in turn allows us to explore how causal or important the STN is in risk-seeking behavior."

To carry out their study, the researchers recruited a group of participants diagnosed with Parkinson's disease who already had electrodes implanted in their brain as part of their clinical treatment. These same electrodes were used to record activity in their STN while they played a computer game.



Drinking game risk task. The figure shows the card game task and stimulation during the decision phase. Credit: Valerie Voon (Figures adapted from *Nature Mental Health* (2024). DOI: 10.1038/s44220-024-00289-z)

"We asked the patients to play an easy card game, which is commonly played as a drinking game," said Voon. "We showed them two decks of cards: one of which was open and the other closed. We then asked them to bet if they thought the next card to be revealed would be higher. If the card they were shown was a low number, such as a 3, they were more likely to bet that the next card would be higher. "

By recording the brain activity of participants as they played this decision-making game, the team could observe what happened in their brains when they expected to win or lose their bets. They could compare the brain activity recorded in instances in which the outcomes are uncertain (e.g., when the card showed to participants was a 4, 5 or 6) to that recorded when the outcomes are far more predictable (e.g., when the card shown was a 1 or 9).

"We were also interested in what we called 'subjective risk' or in other words, what the brain looks like when we are more risk seeking or more risk averse," said Voon. "To explore this question, we stimulated the subthalamic nucleus for 1 second when the patients were trying to make the decision."

The brain wave activity recorded during the team's experiments yielded many interesting insights. Firstly, the researchers observed varying levels of activity in the STN depending on whether participants were expecting to win or lose a bet and on the level of uncertainty associated with a given choice.

"We also showed that this individual subjective tendency towards risk seeking or risk aversion is associated with a different brain wave," Voon explained. "Essentially, our results suggest that the brains of different individuals code what is actually occurring (expecting to win/lose or uncertainty), as well as our actual preferences and tendencies (risk seeking/aversion), differently."

Interestingly, Voon and her research group showed that STN simulation decreased risk seeking. This stimulation was also linked to the increase of a specific frequency (theta 4-8 Hz) in the STN, which when increased led individuals to make safer choices faster.

The sites at which the STN was stimulated also appeared to impact the behavior of participants. Stimulating the higher segment of the STN, known to be linked to movement and typically targeted as part of Parkinson's disease DBS treatments, appeared to influence risk aversion. On the other hand, stimulating the lower part of the STN, linked to emotions and decisions, appeared to increase risk-seeking decisions.

"We know that clinically stimulating these limbic and decision-based regions of the STN can sometimes be associated with a side effect of hypomania which clinically is associated with greater risk seeking," said Voon.

"We have previously already shown that stimulating this region is also associated with feeling more positive emotions, consistent with hypomania. Moreover, we found that different parts in the midline brain are connected to whether we are more risk seeking (the front of the brain) or risk averse (the back of the brain)."

The recent work by this team of researchers shows that activity in the STN varies greatly during risk-related decision-making if an individual is expecting to win, lose or is uncertain about the outcome. This activity also appeared to vary depending on whether individuals are more or less likely to take risks.

"STN stimulation increases risk aversion or the tendency to choose the safe, less risky choice, associated with an increase in a specific brain wave—theta activity," said Voon. "In addition, where we stimulate can have different effects on whether we are more risk seeking or more risk averse."

The findings of this study could soon contribute to the understanding of impulsivity, which is associated with various psychiatric and neurological disorders. Voon and her research group are now trying to use their observations to devise more effective interventions for some of these disorders, as well as decreasing side effects of DBS, such as hypomania.

The researchers are currently recruiting new participants for a DBS study focusing on addiction to opioids and alcohol. This study could provide further insights about the unique neural markers of addiction-related impulsivity.

"I am leading this study between Cambridge, Kings College Hospital and Oxford," Voon added. "As part of these new experiments, we are stimulating two different brain regions involved in reward, motivation and self-control. DBS is very effective for Parkinson's and OCD with preliminary studies suggesting that it might also be effective in addictions. We will run a clinical randomized controlled trial study to look at the efficacy of DBS on addictions."

In their next studies, Voon and her colleagues will focus both on the risk-taking-related processes probed as part of their recent work and on other dimensions of decision-making specifically linked to addiction. These additional dimensions include how the brains of individuals who are addicted to substances respond to alcohol and drug-related triggers, their mood, and other impulsive or compulsive decision-making tendencies.

More information: Valerie Voon et al, Modeling impulsivity and risk aversion in the subthalamic nucleus with deep brain stimulation, *Nature Mental Health* (2024). DOI: 10.1038/s44220-024-00289-z