

NEUROSCIENCE

Brain study seeks roots of suicide

A clinical trial will look at the neurological structure and function of people who have attempted suicide.

BY SARA REARDON

upgrade, the detector had 'rediscovered' a particle called the J/Ψ meson — first found in 1974 by two separate US experiments, and later deemed worthy of a Nobel prize.

In the coming years, CMS and ATLAS are likely to follow in LHCb's footsteps, say Spiropulu and others, and will make the detector algorithms do more work in real time. "That will revolutionize how we do data analysis," says Spiropulu.

An increased reliance on AI decision-making will present new challenges. Unlike LHCb, which focuses mostly on finding known particles so they can be studied in detail, ATLAS and CMS are designed to discover new particles. The idea of throwing away data that could in principle contain huge discoveries, using criteria arrived at by algorithms in a non-transparent way, causes anxiety for many physicists, says Germain. Researchers will want to understand how the algorithms work and to ensure they are based on physics principles, she says. "It's a nightmare for them."

Proponents of the approach will also have to convince their colleagues to abandon tried-and-tested techniques, Gligorov says. "These are huge collaborations, so to get a new method approved, it takes the age of the Universe." LHCb has about 1,000 members; ATLAS and CMS have some 3,000 each.

Despite these challenges, the most hotly discussed issue at the workshop was whether and how particle physics should make use of even more sophisticated AI, in the form of a technique called deep learning. Basic machine-learning algorithms are trained with sample data such as images, and 'told' what each picture shows — a house versus a cat, say. But in deep learning, used by software such as Google Translate and Apple's voice-recognition system Siri, the computer typically receives no such supervision, and finds ways to categorize objects on its own.

Although they emphasized that they would not be comfortable handing over this level of control to an algorithm, several speakers at the CERN workshop discussed how deep learning could be applied to physics. Pierre Baldi, an AI researcher at the University of California, Irvine who has applied machine learning to various branches of science, described how he and his collaborators have done research suggesting that a deep-learning technique known as dark knowledge might aid — fittingly — in the search for dark matter.

Deep learning could even lead to the discovery of particles that no theorist has yet predicted, says CMS member Maurizio Pierini, a CERN staff physicist who co-hosted the workshop. "It could be an insurance policy, just in case the theorist who made the right prediction isn't born yet." ■

Suicide is a puzzle. Less than 10% of people with depression attempt suicide, and about 10% of those who kill themselves have never been diagnosed with any mental-health condition.

Now, a study is trying to determine what happens in the brain when a person attempts suicide, and what sets such people apart. The results could help researchers to understand whether suicide is driven by certain brain biologies — and is not just a symptom of a recognized mental disorder.

The project, which launched in November, will recruit 50 people who have attempted suicide in the 2 weeks before enrolling. Carlos Zarate, a psychiatrist at the US National Institute of Mental Health in Bethesda, Maryland, and his colleagues will compare these people's brain structure and function with those of 40 people who attempted suicide more than a year ago, 40 people with depression or anxiety who have never attempted suicide and a control group of 40 healthy people. In doing so, the researchers hope to elucidate the brain mechanisms associated with the impulse to kill oneself.

Zarate's team will also give ketamine, a psychoactive 'party drug', to the group that has recently attempted suicide. Ketamine, which is sometimes used to treat depression, can quickly arrest suicidal thoughts and behaviour — even in cases in which it does not affect other symptoms of depression¹. The effect is known to last for about a week.

To some researchers, such findings suggest that ketamine affects brain circuits that are specific to suicidal thinking. But John Mann, a psychiatrist at Columbia University in New York City, says that abnormal brain chemistry and genetics could also predispose a person to attempt suicide in times of great stress, such as after a job loss. "They're part of the person, they're a trait," Mann says. "They just get more important when the person gets ill."

There is evidence that genetics influences a person's suicide risk. For instance, biological relatives of adopted children who kill themselves are several times more likely to take their own lives than the general population².

Fabrice Jollant, a psychiatrist at McGill University in Montreal, Canada, suggests that this genetic influence is related to impulsivity and flawed judgement, rather than to a specific mental illness. He has found that close relatives of people who killed themselves were more impulsive than a control group when playing a gambling game designed to test decision-making³. "It seems that this is something transmitted," Jollant says.

Other researchers are seeking biomarkers that would allow clinicians to spot the people most at risk of suicide. Alexander Niculescu, a psychiatrist at Indiana University in Indianapolis, and his colleagues have identified⁴ a set of six genes whose expression is altered in the blood of people who have killed themselves.

The team has found that combining these biomarkers with data from an app that tracks mood and risk factors can predict, with more than 90% accuracy, whether people with bipolar disorder or schizophrenia will eventually be hospitalized for a suicide attempt.

Researchers hope that a better understanding of the biology that underlies suicide will lead to more effective treatments for suicidal impulses. But studies such as Zarate's present difficult logistical and ethical challenges. Researchers must consider whether a person who has just attempted suicide can make informed decisions about whether to participate in research.

Those who study suicidal people say that they treat them with special care — and that the overall benefits of such studies outweigh any risks. "In most clinical trials, people at high risk of suicide are excluded, so we don't know how to treat them," Jollant says. "We need to assess this population, not just say 'exclude them from trials.'" ■

1. Ballard, E. D. *et al. J. Psychiatr. Res.* **58**, 161–166 (2014).
2. Brent, D. A. & Mann, J. J. *Am. J. Med. Genet. C Semin. Med. Genet.* **133C**, 13–24 (2005).
3. Hoehne, A. *et al. J. Psychiatr. Res.* **68**, 192–197 (2015).
4. Niculescu, A. B. *et al. Mol. Psychiatr.* **20**, 1266–1285 (2015).