refractory depression. Nobody, to my knowledge, has actually looked at people who have both conditions.

How do you treat mental health problems in people with IBD?

The most effective way to treat anxiety and depression is behavioural therapy. It's basically a psychological intervention that teaches patients different ways to cope, think and behave, and is effective whether the psychological symptoms occur alone or with another physical condition. My work, the largest randomized controlled trial using cognitive behavioural therapy in adolescents with IBD and depression, showed that cognitive behavioural therapy was more effective than the technique of supportive listening in reducing both depression and inflammation in a subset of people with active IBD.

When the therapy is not enough, my team also uses antidepressants to treat people. There have been a few studies of antidepressants in people with IBD. One tested tricyclic antidepressants for chronic pain in people with IBD or irritable bowel syndrome, and found that the drugs had a positive effect on their pain.

Is there a link between mental health and pain?

Chronic pain in people with IBD is associated with anxiety and depression. About 10% of my patients with IBD have experienced chronic trauma or early life trauma or adversity, and they seem more vulnerable to increased pain perception. The use of narcotics to deal with chronic pain is not uncommon and can be damaging in the long-term, so treatment that takes into account psychological and social factors, as well as biological ones, is really important for people with IBD.

Why would emotional state affect pain?

It's very interesting. In high-resolution functional magnetic resonance imaging studies, researchers have found that the areas where humans process pain are right next to the areas where we process emotions, all the way from lower brain centres up to higher brain centres. As the pain becomes more chronic, studies show that there are more mood swings. So we're thinking about chronic pain as different from just pain that lasts longer.

Where is there hope for people with IBD and psychological issues?

Gut inflammation can be toxic to the brain, especially in people with IBD who have frequent or constant flares of inflammation. We should be focusing more of our attention on developing medications and behavioural interventions that can more specifically change how the inflammation affects both the gut and the brain. ■

INTERVIEW BY NEIL SAVAGE

This interview has been edited for length and clarity.

Q&A Eva Szigethy **Gut feelings**

Many people with inflammatory bowel disease (IBD) also have mental health issues. Eva Szigethy, a psychiatrist at the University of Pittsburgh in Pennsylvania, studies how cognitive therapy can help people with gastrointestinal problems. She spoke to Nature about the relationship between mental health and IBD.

UPMC

What psychiatric issues do you see in people with IBD?

The three major areas that we talk about are anxiety, depression and chronic pain — the pain that persists even when IBD is inactive. There's a subset of adult patients in whom some of the symptoms of depression are caused by the cytokines produced by inflammation that affect the brain. People who have severe IBD will often develop secondary health-related anxiety that leads to avoidance — avoidance of your responsibilities, of your friends and of social opportunities. Often these patients are diagnosed with generalized anxiety disorder.

Are these problems a direct result of IBD?

Compared with healthy populations, anxiety and depression are about twice as high in people with IBD. And the rates are higher when the disease is active compared with when it is inactive. It's still unclear how much of the higher rate of anxiety and depression is specific to IBD and how much it has to do with either the psychological reaction to having a chronic disease or the physical toll of a disease on the brain and the body.

Could mental health problems make people more vulnerable to IBD?

Researchers from Australia recently reviewed studies of depression and anxiety in IBD, and they found that the anxiety seen in most people seemed to precede the diagnosis of IBD. For depression, some studies have shown that

people with IBD had a history of the disorder, but most studies showed the onset of depression occurred after an IBD diagnosis. In children, it seems that most of the anxiety and depression comes after their diagnosis, but adolescence is also the time when anxiety and depression would manifest, so if they happen to have an earlier onset of their IBD it could just be coincidental. Causality and directionality haven't been definitively determined, but there are very strong associations between what happens in the brain and what happens in the gut.

Is there a biological link between mental health problems and inflammation?

In a study of depression subtypes in adolescents with IBD, I showed that you could very convincingly link the somatic or vegetative symptoms of depression — such as fatigue, an inability to feel pleasure, sleep disturbance and low motivation — to the levels of inflammation, using circulating C-reactive proteins or erythrocyte sedimentation rates as markers of systemic inflammation. The cognitive symptoms, such as low self-esteem, suicidal feelings and guilt, are much less correlated with how sick you are with IBD.

The autonomic nervous system links the brain and the gut, and stimulation of that system's biggest branch, the vagus nerve, has recently been shown to be effective in reducing inflammation in people with Crohn's disease. It's interesting because vagal-nerve stimulation is also one of the techniques being used for