Headache, stubbed-toe, injection, broken bone – most of us have suffered pain in one form or another, but our experience of that pain will have varied wildly. In the lab, the same level of stimulation, from extreme cold to electric shock, has been shown to cause a yelp in some but a barely discernible wince in others. Moreover, whereas many people are lucky enough to experience pain as a fleeting encounter, for others pain is a constant companion. The sensitivity and tolerance people show towards pain varies predictably according to several factors, including gender, ethnicity, personality and culture, all interacting, overlapping and playing out in the tissues and synapses of the body. Indeed, the topic of individual differences in pain is like a microcosm of science – it’s where biology, psychology and sociology all meet. So, although the studies that we’ll hear about often focus on either psychosocial or biological mechanisms, it’s worth remembering that a person’s beliefs and cultural upbringing can change the way their body and brain respond to pain. ‘It’s important that we not fight it out as to who’s winning – the psychologists or the biomedical folks,’ says Professor Roger Fillingim, a clinical psychologist at the University of Florida and a leading expert in the field. ‘We need to integrate all of these factors to better understand how they work together to ultimately create the experience of pain.’

Gender

The question of whether men or women have the greater pain threshold is guaranteed to liven up the most soporific of dinner parties. From a lay perspective, evidence exists on both sides. There’s no shortage of stories of feminine bravery – for example, in the grip of prolonged labour. On the other hand, it’s men who have the greater reputation for a warrior instinct and physical risk-taking. Although some studies turn up negative results, the research points overwhelmingly in one direction. Whether in the lab or in the clinic, men demonstrate greater tolerance of and less sensitivity to pain than women. Women are also far more likely to be diagnosed with chronic pain conditions like fibromyalgia (see box). Consider a 1998 paper, typical of the field, in which Pamela Paulson and colleagues scanned the brains of 10 women and 10 men while they experienced a heat stimulus applied to their forearm. The participants were told the experiment was testing their ability to discriminate temperatures using a scale from 0 ‘no heat sensation’ to 10 ‘just barely tolerable pain’. Not only did the female participants consistently rate the higher 50°C stimulus as more painful than the male participants, but their brains also showed a greater change in activation in response to it, including in the 

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extremes of pain

According to the Chronic Pain Policy Coalition over seven million people in the UK are affected by chronic pain and it’s the second most common complaint cited by claimants for incapacity benefit (www.paincoalition.org.uk). Chronic pain can be associated with illnesses such as cancer or arthritis. However at other times, as in the chronic pain syndrome of fibromyalgia, the cause is unclear. Fibromyalgia, which is 10 times more common in women than in men, is typically associated with all-over body pain, increased pain sensitivity and also tenderness on specific parts of the body.

At the other extreme, people with chronic indifference to pain (CIP) lead lives with no experience of pain whatever (Stieg Larsson fans might recall that the unstoppable blond hulk Ronald Niedermann had this diagnosis). CIP may sound like a blessing but the tribulations of those with the condition – undetected bumps, bruises, burns and shortened lifespans – are a reminder of how pain in moderation can serve a useful role. In some cases CIP has been traced to a mutation in a single gene that codes for a protein involved in the sodium channel of nerve endings. A different mutation of the same gene is associated with an opposite condition whereby patients experience even mild touch as excruciatingly painful.

Another form of extreme pain experience is so-called pain synaesthesia. People with this condition have an exaggerated empathy for the sight of other people’s pain. Few cases have been documented so far, but the condition seems to manifest in a person after they themselves have suffered a traumatic pain experience. In a review published in 2010 Bernadette Fitzgibbon cites the case of a man (now deceased) with hyperalgnesia, who experienced physical pain whenever his wife hurt herself. If she knocked her finger, he would grasp his own finger in excruciating pain. Fitzgibbon also describes phantom limb pain triggered in amputees (most of whom had lost their limb in traumatic circumstances) by the sight of other people’s painful experiences or even merely by stories about those experiences.

intake of hormone replacement therapy or the contraceptive pill. Hormones are likely to exert their effects via the inflammatory response, but these pathways are still being worked out. There’s also evidence that the body’s natural pain killer system – the ‘endogenous opioids’ – works differently in women compared with men. For example, in a 2002 study, Jon-Kar Zubieta
and colleagues used PET and a deep-tissue pain stimulation and found less μ-opioid system activation in the brains of female compared with male participants. Men and women respond differently to pain treatments too, with women generally showing more of a response to opioid-based analgesics, although this research is patchy.

There are also cognitive factors that could explain gender differences in pain response. One of these concerns ‘catastrophising’ – that is, perceiving a pain as particularly threatening and believing that it is too severe to cope with. Typical items used to measure this factor include: ‘it is terrible and I feel it is never going to get any better’ and ‘it is awful and I feel it overwhelms me’.

Several studies have shown that women tend to catastrophise about pain more than men. In 2000, for example, when Francis Keefe at the Duke University Medical Centre and his team studied 168 patients with osteoarthritis of the knees, they found that the female patients reported more pain but that this gender difference disappeared once levels of catastrophising were taken into account.

Ethnicity
Alongside gender, substantial evidence has also accumulated suggesting an association between pain experience and ethnicity. Generally, white Caucasian people are found to be less sensitive to, and more tolerant of, pain than individuals of African or Asian descent.

Claudia Campbell and colleagues in association with Fillingim’s Lab at the University of Florida, for example, reported in 2005 that 62 African American participants were on average less tolerant of heat pain, cold pressor pain and ischaemic pain than white participants. Another study by the same research team found that African American participants exhibited the nociceptive flexion reflex – an automatic withdrawal movement – to an electrical pain stimulus at a lower intensity than did white participants. This paradigm has the advantage of not requiring participants to report the pain they’re experiencing, so bypassing some of the socio-cultural confounds that that entails.

Although most studies in this field have compared African Americans and white Americans, there are some exceptions. Osamu Komiya’s team at the Nihon University School of Dentistry at Matsudo, for example, compared white Caucasian Belgian and Japanese participants, finding that the latter were more sensitive to needle-like stimuli applied to their cheek, gums or tongue. Intriguingly, this same study also found that, despite their increased sensitivity, the Japanese participants gave the same stimuli lower pain ratings. The researchers said this likely reflects the Japanese cultural emphasis on stoicism and the desirability of concealing pain and emotions’ (see ‘Cultural differences’).

Besides the role played by cultural influences, several physiological and psychological mechanisms underlying ethnic differences have also been identified. One of these is the endogenous pain control mechanism called ‘diffuse noxious inhibitory controls’. This is the physiological reality behind the folk belief that one way to alleviate an ache is to induce pain somewhere else in the body.

Another study by Claudia Campbell and colleagues in 2008 investigated this in relation to an ischaemic pain, induced via a tightened arm tourniquet, and a painful electric zap to the leg. In the wake of the arm pain, white participants showed greater reductions in sensitivity to the electric stimulation to their leg than did African American participants.

As regards psychosocial factors, a team led by F Bridgett Rahim-Williams in Roger Fillingim’s lab found that pain sensitivity was greater among African Americans and Hispanics who expressed more identification with their ethnic group – for example, they agreed with statements like ‘I’ve spent time trying to find out more about the history and traditions of my ethnic group’. Consistent with this, Ben Palmer and colleagues at Manchester University Medical School and the University of Aberdeen found that reports of all-over body pain were four times higher, on average, among a sample of South Asian participants in the UK compared with white Europeans, and crucially, that such reports were negatively correlated with participants’ degree of assimilation into British culture.

One possible explanation for these effects of ethnic identification and assimilation is that ethnic differences in pain experience are largely cultural and so people who identify more with their ethnic group are more likely to be susceptible to these cultural influences. Again it’s important to remember that cultural influences are also likely to have neurobiological correlates, as a person’s...
Cultural differences

‘between death and shame, death has the greater beauty’

These lines come from a Bariba proverb quoted in a 1984 article by the anthropologist Carolyn Sargent, now at Washington University in St Louis. The Bariba are an ethnic group located in Benin and Nigeria in West Africa and whenever Sargent attempted to talk to them about pain, she found that they turned the discussion to issues of honour and shame, many of them citing the proverb above. The Bariba, at least at the time of Sargent’s study, believed that expressions of pain were a shameful sign of weakness. Boys were circumcised in groups and taught not to show a flicker of pain. Girls too were circumcised but were allowed to cry. Women were expected to deliver their own babies and any outward signs of pain were considered taboo. Do these behavioural mores have any influence on pain perception? Bariba women told Sargent that there was pain in labour but there was no point in crying – if you’re going to die it won’t help, they said. Recalling her clitoridectomy as child (a practice that has since been outlawed) another woman told Sargent that no pain is as excruciating and that after that experience no pain will ever overwhelm a person.

Several psychologists investigating cross-cultural attitudes to pain have used the ‘Appropriate Pain Behaviour Questionnaire’, which includes items such as ‘Men (or women) should be able to tolerate pain in most circumstances’ or ‘It is acceptable for men (or women) to cry when in pain.’ Using this questionnaire in a 2005 study, Mieko Hobara at the New York State Psychiatric Institute found that 32 Japanese men and women consistently rated it as less appropriate for people of either gender to express pain compared with 32 Euro-American men and women. Using the same scale in a 2000 study, Sangeetha Nayak and colleagues found that college students in India similarly rated expressions of pain as less acceptable than their counterparts in the USA. In line with their beliefs, the Indian participants also showed greater pain tolerance than the US sample.

Other researchers have examined differences between cultures in their linguistic terms for pain. Anthony Diller writing in 1980 noted that some languages have one general term for pain which is then tailored with modifiers – for example, sharp pain or stinging pain – whereas other languages, such as Thai, have several different words that refer directly to different types of pain. He also notes that the Khamti language of Assam in India has four different words for itchy and that the Japanese have different terms for pain depending on the status of the sufferer.

Personality

Another major factor that’s associated with the way a person experiences pain is personality. Although research in this area is hampered by the use of varied personality measures, a consistent finding is that people who score higher on neuroticism or a neuroticism-like factor tend to show greater sensitivity to pain and reduced tolerance. Helen Vossen at Maastricht University in a 2006 paper showed this sensitivity is also reflected in an exaggerated cortical response to pain as measured by EEG in an electrical pain paradigm. Aspects of personality also seem to predict the way a person responds to pain relief. Don’t Pud of the Pain Relief Unit at the Rambam Medical Centre in Israel found that men and women who scored more highly on ‘harm avoidance’ (a trait resembling ‘neuroticism’ that’s derived from Robert Cloninger’s Tridimensional Personality Questionnaire) showed a larger response to morphine in terms of their subsequent performance on the cold pressor task.

Personality isn’t only related to acute pain sensitivity and tolerance, it’s also predictive of chronic pain conditions in later life, and people diagnosed with a chronic pain condition tend to exhibit a characteristic personality profile. For instance, Katherine Applegate and colleagues at Duke University Medical Centre caught up with over 2000 university students after a 30-year gap and found that those who’d scored highly in their youth on the Minnesota Multiphasic Personality Inventory measures of ‘femininity’ (male participants only), ‘paranoia’ (female participants only), ‘hypochondriasis’, or ‘hysteria’ also tended to be more likely to have a chronic pain condition in middle age.

As for the typical character profile of a chronic pain patient, Rupert Conrad at the University of Bonn in a 2007 paper compared 207 patients with 105 pain-free controls, finding that the patients scored higher on ‘harm avoidance’ and lower on ‘self-directedness’ (a mix of the Big Five factors of Conscientiousness and Extraversion) and ‘cooperativeness’ (akin to the Big Five factor of Agreeableness). The patients also tended to score higher on depression and state anxiety; with 41 per cent meeting the psychiatric criteria for a personality disorder (PD) – most frequently paranoid or borderline PD.

It’s obviously sensible to take rest, relax and take precautions after a painful injury. However, Conrad says a person who scores high in harm avoidance will
special issue

continue to behave in this way even after their injury has healed. He adds that a related personality factor associated with chronic pain is low self-efficacy. ‘That means a feeling of helplessness and a conviction of not being capable of controlling a situation or being able to overcome obstacles associated with chronic pain.’

‘As a consequence,’ he explains, ‘chronic pain treatment should aim at psychological mechanisms enhancing self-efficacy and lessen avoidance (e.g. cognitive behavioural therapy) and at pharmacologic agents improving supraspinal modulation of pain. It is important to note that psychotherapeutic and pharmacologic approaches should be seen as complementary treatments.’

Somewhat paradoxically, whilst the prevalence of borderline PD is elevated among patients diagnosed with a chronic pain condition, the same diagnosis is also associated with reduced pain sensitivity on laboratory measures. In one representative study published in 2004, Christian Schmahl at Johannes Gutenberg-University used an infrared laser as the painful stimulus and found 10 women diagnosed with borderline PD to have higher heat pain thresholds and lower subject pain ratings than 14 non-clinical controls. In 2006 the same researcher and his team linked this reduced pain sensitivity to reduced pain-related activation in the anterior cingulate gyrus and amygdala of patients with borderline PD compared with controls.

Recently attention has turned to identifying the physiological mechanisms, not merely the neural correlates, that might account for the link between personality and pain perception. Two years ago, in an unpleasant-sounding experimental paradigm, Peter Patine and colleagues at Hope Hospital in Manchester identified a link between personality, pain and autonomic nervous system activity. They used a balloon inflated in the oesophagus to simulate visceral pain and found that this triggered an increase in parasympathetic nervous system activity, as identified through heart-rate variability, in participants who scored more highly in neuroticism, whereas repetitions of the same stimulus in those lower in neuroticism led to reduced parasympathetic activity. One possible explanation is that increased parasympathetic nervous system activity corresponds to a ‘freeze’ response in the participants higher in neuroticism, although how this relates to pain experience remains to be worked out.

Conrad says there’s evidence that the personality factors underlying chronic pain may be associated with decreased activation of the prefrontal cortex – a key brain region involved in the top-down modulation of pain. This neuroanatomical structure can be activated by a cognitive anticipation of the potential controllability of pain, he says. ‘A personality-based conviction of uncontrollability and helplessness and an avoidance of pain makes activation of these neuroanatomical structures less likely and hampers top-down modulation of pain.’

Applications and controversies

We’ve seen how factors like ethnicity and personality are related to people’s experience of pain, a key challenge now is to use this information to improve people’s quality of life. ‘The goal ultimately,’ says Fillingim ‘is to gather all the information we have about an individual – their age, weight, race, sex, genotype data, psychology questionnaire results – put all that into a computer and based on an abundance of evidence that we already have, the computer will tell us, for example, what drug is going to work best for that person.’ And even more helpful, Fillingim says, is that same information might help predict who’s at risk for developing chronic pain. For example, if it’s judged that a patient has a high chance of developing a chronic pain condition after surgery, it might be better to pursue alternative treatment options where they exist. ‘So, it’s not just picking the right drug or dose,’ Fillingim says, ‘it’s really understanding the risk for the development of chronic pain because chronic pain is what we really have trouble helping people with.’

Conrad agrees, adding: ‘Future studies addressing the issue of chronic pain have to give an even deeper insight into the complex interplay of personality factors, psychological mechanisms and the associated neurobiological mechanisms. The identification of a risk factor such as low self-efficacy by personality questionnaires – for example, temperament and character inventory – may lead to an earlier identification of populations at risk and may lead to an earlier treatment, which may positively affect outcomes.

‘How long until these kind of benefits might be seen? I’m sure we’ll get there one day,’ Fillingim says, ‘but I’m not sure how far away that is. The more we get into these individual differences, be it genetic, gender, ethnic group or whatever, the more complicated everything looks!’

A particularly compelling justification for continuing to study individual differences in pain experience comes from as yet unpublished research looking at genetic influences on pain perception. Fillingim and his colleagues have identified a marker for a particular gene that’s associated with increased pain sensitivity in one ethnic group but reduced pain sensitivity in another. ‘This means that if biomedical researchers ignore factors like ethnicity and gender, they risk forming conclusions about genetic influences that are too general,’ says Fillingim. ‘This just shows that we’ve got a lot of work to do,’ says Fillingim, ‘but hopefully it will be useful in the long run.’

Inevitably perhaps, this field has attracted criticism from those who fear the findings will be used to bolster stereotypes. Fillingim and others in the field are sensitive to these concerns and don’t want their results to be used in that way. ‘To me the broader concern is with health disparities such that ethnic groups experience poorer health than white people do – that’s obviously driven by many factors including socio-economic status but what we’re finding may imply that there are individual characteristics of people from different ethnic groups making them more or less prone to experiencing pain or disability associated with pain, and unless we understand what’s driving these differences, we’re not going to be able to remove the health disparities even if we fix all the system-level problems. So I think the benefits of this kind of research far outweigh the concerns that people have.’

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