



Francis McGlone.

# A touching story

C-tactile fibres in hairy skin, specialised for responding to gentle stroking, could be playing a key role in development of the social brain.

Unmyelinated C-fibres are the 'slow train' conveying sensory signals to the brain. Perhaps best known are the C-fibres that convey nociceptive signals and trigger the emotional responses accompanying painful stimuli. But, points out **Francis McGlone** at Liverpool John Moores University, human skin also has C-fibres dedicated to itch, and others – C-tactile fibres – responsive to gentle touch. And evidence is accumulating that the C-tactile fibre system could have a profound impact on human development and biology.

Recent years have seen growing interest in human C-tactile fibres, although mechanoreceptors sensitive to gentle stroking – 'C low-threshold mechanoreceptors' (CLTM) – were first discovered in cat cutaneous sensory nerves in the 1930s. The fibre has since been found in all social mammals studied, says Professor McGlone, although its significance has been unclear: "It's taken a long time to understand what it is there for."

His interest in C-tactile fibres, the human equivalent of CLTM, emerged during his time in industry. "I was the most fortunate man on the planet in those days, because Unilever had an exploratory research group whereby they stripped away 10% of its annual R&D budget, and provided it to scientists to build new science."

Unilever produced grooming and cleaning products but Professor McGlone realised that grooming was not just about hygiene – it was perceived as pleasant and hence rewarding: "It's not to look good, it's to feel good," he suggests. Indeed, he had shown that gentle stroking was perceived as pleasant, and catching up on his reading during a transatlantic flight he came across the reason why: "I was sat on an airplane flying out of Washington and reading a paper by Ake Vallbo describing the characteristics of the C-tactile fibre that responded to gentle touch and everything became crystal clear."

The palm of the hand (glabrous skin) is packed full of myelinated mechanoreceptors. "The fast nerves have dominated our understanding of touch," says Professor McGlone. "That's where most people consider touch to be. The glabrous skin is basically exploring the outside world – it's haptics, it's object recognition. But that's the boring stuff. The rest of the body, that's where the C-tactile fibres are."

To get at their function, Professor McGlone's lab is the only one in the country using

microneurography to record from single peripheral nerves – a painstakingly difficult technique – as well as intraneural microstimulation to probe individual units. He has also developed techniques for combining these approaches with functional imaging and magnetoencephalography.

These approaches have provided a pleasing correlation between psychophysical and electrophysiological studies – slow stroking is perceived as most pleasant and C-tactile fibres are tuned precisely to this frequency of stimulation.

## The purpose of touch

From an evolutionary perspective, the function of nociceptor C-fibres is of obvious survival benefit. But what is the point of a sensory system responsive to gentle touch? For Professor McGlone, the answer lies in social bonding, with the pleasant and rewarding sensation of C-tactile fibre stimulation encouraging close physical contact.

This idea, points out Professor McGlone, ties together a multitude of seemingly disparate observations. "There's a whole litany of observations where no one has put one and one together to make two."

In the animal world, the importance of grooming to social bonding is well recognised. Furthermore, maternal grooming plays a critical role in mouse development – mice that are not groomed by mothers when young show a range of abnormal stress responses and behaviours.

A neurodevelopmental role for C-tactile fibres could also provide an explanation for the apparent benefits of close contact between young babies and mothers. Anthropological studies have provided suggestive evidence of the calming effect of extensive close contact (inspiring the so-called 'baby-wearing' movement). And 'kangaroo mother care' – skin-to-skin contact for premature babies – has been shown to have remarkably beneficial effects on infant health and development. Although endorsed by the WHO, the mechanisms underlying these benefits are unclear, but could conceivably reflect stimulation of C-tactile fibres.

Further circumstantial evidence for the potential importance of the C-tactile fibre system comes from neonatal intensive care units, where early touch between mother and infant is obviously limited. Around one in four such infants go on to develop autism. In addition, groups who have



Using microneurography and EEG to probe C-tactile fibre function.

endured serious neglect as infants, such as Romanian orphans from the Ceausescu era, also show high levels of autism spectrum disorder (and other neurocognitive disorders).

Indeed, Professor McGlone highlights other possible links between C-tactile fibres and autism. Many people with autism find gentle touch uncomfortable, hinting at underlying abnormalities in C-tactile fibre systems. Furthermore, he has pondered what might happen developmentally in the absence of C-tactile fibres: “It would look like this thing we call autism,” he suggests. His work with Kevin Pelphry at Yale has revealed that C-tactile fibres are less responsive to touch in young people with autism, which could potentially contribute to reduced capacity for social bonding.

The more he has studied C-tactile fibres, the more convinced he has become of their neurodevelopmental importance – and hence the value of regular physical contact between young people and caregivers. He is increasingly alarmed at the growing trend to restrict physical contacts, particularly in environments such as the classroom. An unfortunate consequence of overblown fears of sexual abuse could be a reduction in the physical contact required for development of the social brain and interpersonal relationships.

Touch is also important in adults. The pleasurable effects of massage, for example, are well known. Practitioners may have developed a range of fanciful narratives to explain these effects but, suggests Professor McGlone, they rely on more prosaic neurophysiology: “It doesn’t matter what story you tell, the nerve fibres have worked it out.” Notably, massage often focuses on the back and shoulders – precisely the areas known to be most densely innervated by CTLM in animals.

### Exploring the role of C-tactile fibres

Looking forward, Professor McGlone is keen to understand exactly what C-tactile fibre signalling is doing to the brain. He is particularly keen to examine its effects on serotonergic pathways, as depression is yet another condition where C-tactile fibres may be playing a role – people with depression typically have less human contact. With a US group licensed to administer MDMA, he will also be exploring whether the drug makes stroking seem more pleasurable, which could help to explain why ecstasy use is associated with a craving for physical contact.

He is also working on a schools-based project, exploring the impact of a peer-to-peer massage programme. Empirically, several schools have found that the activity, in which pairs of students rub each other’s backs, has a marked impact on students’ behaviour: “The teachers recognise that those kids are far calmer, far more relaxed and for more easy to manage,” says Professor McGlone. He is organising a controlled trial comparing the massage with paired reading sessions, using cortisol levels before a simulated maths exam to assess students’ stress responses.

In the medical arena, he is collaborating with colleagues in Italy on a trial examining the impact of stroking in neonatal intensive care units. He is also working with Rebecca Slater in Oxford to explore the impact of stroking on babies’ responses to heel pricks.

More generally, he is spreading the word about the potential importance of C-tactile fibres, for example through the International Association for the Study of Affective Touch (IASAT), which held its second meeting in Liverpool in September 2017. Like pain, another research area he has worked in extensively, gentle touch spans multiple fields, from neurophysiology to the social sciences. Indeed, he suggests, many more people would benefit from focusing on C-tactile fibres: “A lot of people who didn’t know this fibre exists, when you tell them about it they say ‘ahhh...’ – they think that’s really interesting and then they start reinterpreting their own data. It’s surprising after all these years how so few people seem to know about this enigmatic nerve fibre.”

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