Are these the brain cells that give us consciousness?

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The brainiest creatures share a secret – an odd kind of brain cell involved in emotions and empathy that may have accidentally made us conscious

THE origin of consciousness has to be one of the biggest mysteries of all time, occupying philosophers and scientists for generations. So it is strange to think that a little-known neuroscientist called Constantin von Economo might have unearthed an important clue nearly 90 years ago.

When he peered down the lens of his microscope in 1926, von Economo saw a handful of brain cells that were long, spindly and much larger than those around them. In fact, they looked so out of place that at first he thought they were a sign of some kind of disease. But the more brains he looked at, the more of these peculiar cells he found - and always in the same two small areas that evolved to process smells and flavours.

Von Economo briefly pondered what these "rod and corkscrew cells", as he called them, might be doing, but without the technology to delve much deeper he soon moved on to more promising lines of enquiry.

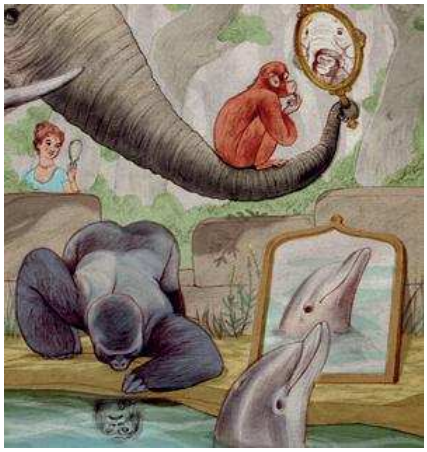
Little more was said about these neurons until nearly 80 years later when, Esther Nimchinsky and Patrick Hof at Mount Sinai University in New York also stumbled across clusters of these strange-looking neurons. Now, after more than a decade of functional imaging and post-mortem studies, we are beginning to piece together their story. Certain lines of evidence hint that they may help build the rich inner life we call consciousness, including emotions, our sense of self, empathy and our ability to navigate social relationships.

Many other big-brained, social animals also seem to share these cells, in the same spots as the human brain. A greater understanding of the way these paths converged could therefore tell us much about the evolution of the mind.

Admittedly, to the untrained eye these giant brain cells, now known as von Economo neurons (VENs), don't look particularly exciting. But to a neuroscientist they stand out like a sore thumb. For one thing, VENs are at least 50 per cent, and sometimes up to 200 per cent, larger than typical human neurons. And while most neurons have a pyramid-shaped body with a finely branched tree of connections called dendrites at each end of the cell, VENs have a longer, spindly cell body with a single projection at each end with very few branches (see diagram). Perhaps they escaped attention for so long because they are so rare, making up just 1 per cent of the neurons in the two small areas of the human brain: the anterior cingulate cortex (ACC) and the fronto-insular (FI) cortex.

Their location in those regions suggests that VENs may be a central part of our mental machinery, since the ACC and FI are heavily involved in many of the more advanced aspects of our inner lives. Both areas kick into action when we see socially relevant cues, be it a frowning face, a grimace of pain or simply the voice of someone we love. When a mother hears a baby crying, both regions respond strongly. They also light up when we experience emotions such as love, lust, anger and grief. For John Allman, a neuroanatomist at the California Institute of Technology in Pasadena, this adds up to a kind of "social monitoring network" that keeps track of social cues and allows us to alter our behaviour accordingly (*Annals of the New York Academy of Sciences*, vol 1225, p 59).

The two brain areas also seem to play a key role in the "salience" network, which keeps a subconscious tally of what is going on around us and directs our attention to the most pressing events, as well as monitoring sensations from the body to detect any changes (*Brain Structure and Function*, DOI:



The consciousness connection *(Image: Jonathon Burton)*

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What's more, both regions are active when a person recognises their reflection in the mirror, suggesting that these parts of the brain underlie our sense of self - a key component of consciousness. "It is the sense of self at every possible level - so the sense of identity, this is me, and the sense of identity of others and how you understand others. That goes to the concept of empathy and theory of mind," says Hof.

To Bud Craig, a neuroanatomist at Barrow Neurological Institute in Phoenix, Arizona, it all amounts to a continually updated sense of "how I feel now": the ACC and FI take inputs from the body and tie them together with social cues, thoughts and emotions to quickly and efficiently alter our behaviour (*Nature Reviews Neuroscience*, vol 10, p 59).

This constantly shifting picture of how we feel may contribute to the way we perceive the passage of time. When something emotionally important is happening, Craig proposes, there is more to process, and because of this time seems to speed up. Conversely, when less is going on we update our view of the world less frequently, so time seems to pass more slowly.

VENs are probably important in all this, though we can only infer their role through circumstantial evidence. That's because locating these cells, and then measuring their activity in a living brain hasn't yet been possible. But their unusual appearance is a signal that they probably aren't just sitting there doing nothing. "They stand out anatomically," says Allman, "And a general proposition is that anything that's so distinctive looking must have a distinct function."

Fast thinking

In the brain, big usually means fast, so Allman suggests that VENs could be acting as a fast relay system - a kind of social superhighway - which allows the gist of the situation to move quickly through the brain, enabling us to react intuitively on the hop, a crucial survival skill in a social species like ours. "That's what all of civilisation is based on: our ability to communicate socially, efficiently," adds Craig.

A particularly distressing form of dementia that can strike people as early as their 30s supports this idea. People who develop fronto-temporal dementia lose large numbers of VENs in the ACC and FI early in the disease, when the main symptom is a complete loss of social awareness, empathy and self-control. "They don't have normal empathic responses to situations that would normally make you disgusted or sad," says Hof. "You can show them horrible pictures of an accident and they just don't blink. They will say 'oh, yes, it's an accident'."

Post-mortem examinations of the brains of people with autism also bolster the idea that VENs lie at the heart of our emotions and empathy. According to one recent study, people with autism may fall into two groups: some have too few VENs, perhaps meaning that they don't have the necessary wiring to process social cues, while others have far too many (*Acta Neuropathologica*, vol 118, p 673). The latter group would seem to fit with one recent theory of autism, which proposes that the symptoms may arise from an over-wiring of the brain. Perhaps having too many VENs makes emotional systems fire too intensely, causing people with autism to feel overwhelmed, as many say they do.

Another recent study found that people with schizophrenia who committed suicide had significantly more VENs in their ACC than schizophrenics who died of other causes. The researchers suggest that the over-abundance of VENs might create an overactive emotional system that leaves them prone to negative self-assessment and feelings of guilt and hopelessness (*PLoS One*, vol 6, p e20936).

VENs in other animals provide some clues, too. When these neurons were first identified, there was the glimmer of hope that we might have found one of the key evolutionary changes, unique to humankind, that could explain our social intelligence. But the earliest studies put paid to that kind of thinking, when VENs turned up in chimpanzees and gorillas. In recent years, they have also been found in elephants and some whales and dolphins.

Like us, many of these species live in big social groups and show signs of the same kind of advanced behaviour associated with VENs in people. Elephants, for instance, display something that looks a lot like empathy: they work together to help injured, lost or trapped elephants, for example. They even seem to show signs of grief at elephant "graveyards" (*Biology Letters*, vol 2, p 26). What's more, many of these species can recognise themselves in the mirror, which is usually taken as a rudimentary measure of consciousness. When researchers daub paint on an elephant's face, for instance, it will notice the mark in the mirror and try to feel the spot with its trunk. This has led Allman and others to speculate that von Economo neurons might be a vital adaptation in large brains for keeping track of social situations - and that the sense of self may be a consequence of

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this ability.

Yet VENs also crop up in manatees, hippos and giraffes - not renowned for their busy social lives. The cells have also been spotted in macaques, which don't reliably pass the mirror test, although they are social animals. Although this seems to put a major spanner in the works for those who claim that the cells are crucial for advanced cognition, it could also be that these creatures are showing the precursors of the finely tuned cells found in highly social species. "I think that there are homologues of VENs in all mammals," says Allman. "That's not to say they're shaped the same way but they are located in an analogous bit of cortex and they are expressing the same genes."

It would make sense, after all, that whales and primates might both have recycled, and refined, older machinery present in a common ancestor rather than independently evolving the same mechanism. Much more research is needed, however, to work out the anatomical differences and the functions of these cells in the different animals.

That work might even help us understand how these neurons evolved in the first place. Allman already has some ideas about where they came from. Our VENs reside in a region of the brain that evolved to integrate taste and smell, so he suggests that many of the traits now associated with the FI evolved from the simple act of deciding whether food is good to eat or likely to make your ill. When reaching that decision, he says, the quicker the "gut" reaction kicks in the better. And if you can detect this process in others, so much the better.

"One of the important functions that seems to reside in the FI has to do with empathy," he says. "My take on this is that empathy arose in the context of shared food - it's very important to observe if members of your social group are becoming ill as a result of eating something." The basic feeding circuitry, including the rudimentary VENs, may then have been co-opted by some species to work in other situations that involve a decision, like working out if a person is trustworthy or to be avoided. "So when we have a feeling, whether it be about a foodstuff or situation or another person, I think that engages the circuitry in the fronto-insular cortex and the VENS are one of the outputs of that circuitry," says Allman.

Allman's genetics work suggests he may be on to something. His team found that VENs in one part of the FI are expressing the genes for hormones that regulate appetite. There are also a lot of studies showing links between smell and taste and the feelings of strong emotions. Our physical reaction to something we find morally disgusting, for example, is more or less identical to our reaction to a bitter taste, suggesting they may share common brain wiring (*Science*, vol 323, p 1222). Other work has shown that judging a morally questionable act, such as theft, while smelling something disgusting leads to harsher moral judgements (*Personality and Social Psychology Bulletin*, vol 34, p 1096). What's more, Allman points out that our language is loaded with analogies - we might find an experience "delicious", say, or a person "nauseating". This is no accident, he says.

Red herring

However, it is only in highly social animals that VENs live exclusively in the scent and taste regions. In the others, like giraffes and hippos, VENs seem to be sprinkled all over the brain. Allman, however, points out that these findings may be a red herring, since without understanding the genes they express, or their function, we can't even be sure how closely these cells relate to human VENs. They may even be a different kind of cell that just looks similar.

Based on the evidence so far, however, Hof thinks that the ancestral VENs would have been more widespread, as seen in the hippo brain, and that over the course of evolution they then migrated to the ACC and FI in some animals, but not others - though he admits to having no idea why that might be. He suspects the pressures that shaped the primate brain may have been very different to those that drove the evolution of whales and dolphins.

Craig has hit upon one possibility that would seem to fit all of these big-brained animals. He points out that the bigger the brain, the more energy it takes to run, so it is crucial that it operates as efficiently as possible. A system that continually monitors the environment and the people or animals in it would therefore be an asset, allowing you to adapt quickly to a situation to save as much energy as possible. "Evolution produced an energy calculation system that incorporated not just the sensory inputs from the body but the sensory inputs from the brain," Craig says. And the fact that we are constantly updating this picture of "how I feel now" has an interesting and very useful by-product: we have a concept that there is an "I" to do the feeling. "Evolution produced a very efficient moment-by-moment calculation of energy utilisation and that had an epiphenomenon, a by-product that provided a subjective representation of my feelings."

If he's right - and there is a long way to go before we can be sure - it raises a very humbling possibility: that far from being the pinnacle of brain evolution,

consciousness might have been a big, and very successful accident.

This article has been edited since it was first posted

***Caroline Williams** is a writer based in Surrey, UK*

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