Twilight in the Box

By Shurti Ravindran

The suicide statistics, squalor & recidivism haven't ended solitary confinement. Maybe the brain studies will.

You are where you live. How you live shapes who you are. We owe a debt to the Canadian neuropsychologist Donald O Hebb for proving these aphorisms right down to the neurone. In 1947, Hebb took a few rat pups home for his children to play with. When these pups grew older and hairier, and were less welcome darting about the furniture, he brought them back to his McGill University lab, where they outsmarted cage-reared rats in problem-solving tests. They were also visibly well-adjusted, unlike cage-bound compatriots who groomed themselves until their whiskers dropped off, and had balding patches all over their bodies.

During the 1960s and '70s, researchers at the University of California, Berkeley, followed up on Hebb's intriguing observation with controlled experiments in the lab. The neuroscientist Mark Rosenzweig showed that, when compared with rat packs that roved in rodent McMansions filled with ladders, tunnels and toys, animals that languished in spartan, supermax-style cages had fewer connections between neurons and thinner cerebral cortexes. Marian Diamond, a colleague of Rosenzweig, showed that various types of enriched or impoverished environmental exposures could alter the dimensions and even the cellular content of the cortex at any age from newborn to elderly. Even four days of impoverished environment could have an impact on the physiology of the cortex and its ability to navigate the world.

These were stunning discoveries. The cerebral cortex, what we refer to as 'grey matter', is the part of the brain that makes us most human. This dime-thick, intricate surface runs across the two hemispheres of our brain. It's where we make our plans, guide our movements and consciously respond to social cues. It's where stimulus turns to perception, where the neural nuts-and-bolts of language reside. The Berkeley

experiments showed that, at least for rats, social interactions and surroundings are inscribed in the neurophysiology of the brain, and not just during the early part of life.

As years passed, an irrefutable body of work in a range of species established that social interactions across complex terrain could nourish and boost the brain, while impoverished surroundings diminished it in every stage of life. By the 1980s, the neuroscientist Fernando Nottebohm of Rockefeller University was reporting the growth of new neurons whenever adult songbirds learnt new songs. Later, he examined the sea-horse-shaped hippocampus, a seat of spatial memory, in the brains of adult black-capped chickadees. Captive chickadees, he found, generated fewer new neurons in their hippocampi compared with counterparts from the wild.

By 1998, a team at the Salk Institute in California had connected social interaction and play to improved episodic memory and mood – and enhanced desire to venture out and explore. To do their work, the Salk team corralled 12 mice in a lavishly equipped cage fitted with tunnels, toys, and a running wheel, while a control group of four mice were consigned to a plastic box shanty. A month later, the mice were thrown into a Morris maze – a circular tub of water with a submerged platform in the middle. Those who'd had the benefit of play facilities managed to locate the resting spot more rapidly than their deprived peers. Meanwhile, two matching groups of mice were injected with a chemical marker that stained new neurons red. Compared with their confined counterparts, mice in the enriched environment had hippocampi teeming with many more brain cells, including neurons and astroglia, which help new neurons survive. Of special note, the enriched mice had 57 per cent more new nerve cells in their dentate gyrus – a corner of the hippocampus that helps consolidate episodic memory, control depression and stress, and spur exploration of new environments.

But what was it about isolation and confinement that caused the brain to become impoverished? In 2004, the Princeton neuroscientist Elizabeth Gould and postdoctoral researcher Alexis Stranahan inadvertently stumbled upon a clue while investigating a paradox: exercise was known to release stress hormones that should tamp down on

neural growth. Yet a raft of studies consistently showed that exercise was a fail-safe way of enhancing the growth of new neurons in the adult brain.

To investigate, Stranahan and Gould took adult rats, housed separately, and had them scrabble around running wheels. Then Stranahan killed the rats and examined their brains under the microscope. She was dismayed to find no increase in neurogenesis in spite of the exercise. ‘Not only that, she saw an opposite effect,’ Gould told me. ‘The running animals were showing a reduction in neurogenesis.’ When Stranahan consulted the studies she’d been trying to replicate, she saw that all prior test subjects had been group-housed.

On closer scrutiny, Gould and Stranahan found that when the adult rats who’d been isolated ran, their brains were flush with elevated levels of the stress hormone corticosterone – the rodent analogue of the human stress hormone cortisol, produced by the adrenal gland. Isolation had caused levels of the hormone to spike so high that, instead of proliferating, neurons were dying off. In fact, the isolated rats’ brains could spawn new neurons only when stress hormones were forcibly lowered by removing the adrenal glands. ‘It shows that when animals live alone, they’re not very good at coping with a challenge [such as running] to the system,’ says Gould.

At the root of all of this, it turns out, is stress itself. Under normal circumstances, the brain keeps stress in check through an intricate set of feedback loops between the endocrine, nervous and immune system. We owe this balance, a state called ‘homeostasis’, to a set of unseen thermostats humming within us, maintaining stability through adjustments to such set points as body temperature or the oxygen levels of our blood. But when the environment throws a wrench in the works, another system comes into play. The core conductor here is what neuroscientists call the hypothalamic-pituitary-adrenal (HPA) axis, a network of organs fuelling our most ancient, atavistic urges: to fight or take flight.

When something triggers a fire alarm, the almond-sized hypothalamus deep within the brain dispatches an urgent message to the adrenal glands atop the kidneys, which

respond by seeping out the stress hormone adrenalin. This speeds up the heart rate, flushing more blood into muscles and organs, and sending oxygen billowing into the lungs and the brain, keeping us alert and sharpening our senses. These processes encourage us to meet our challenges head-on, whether it's getting out of bed, fleeing a predator, or conducting an orchestra.

If the threat continues, the hypothalamus releases a substance called corticotrophin-releasing factor. This rushes to the pituitary, a tiny gland at the top of the brain, which in turn, produces adrenocorticotropic hormone (ACTH). ACTH surges to the adrenal glands, which release another stress hormone, cortisol, into the blood. Cortisol converts protein to fat, catalysing the production of energy and releasing minerals from our bones. This makes up for the energy we lost in the adrenalin rush, and it also makes us active and hungry. Meanwhile, after the threat has passed, a calming infusion of neurotransmitters – serotonin, dopamine, noradrenaline – flows to temper the stress response, and restore homeostasis once again.

A little stress-induced cortisol is actually good for you. It reins in the immune system, controls inflammation, and keeps you alert and energised in the morning when its levels are naturally high. But when stress is chronic, the ebb and flow of stress hormones becomes a steady, unceasing seep. The hippocampus is not able to shut down the stress response, leading to weakened immunity, demineralised bones, clogged and narrowed arteries, obesity, impaired memory and cognition, and a susceptibility to psychological problems. Chronically depressed people are likely to have too much cortisol sloshing around their brain through the day, while sufferers of post-traumatic stress disorder (PTSD) – and residents of the Box – likely owe their constant state of hypervigilance to overpowering doses of noradrenaline.

Some of the most crucial discoveries about how stress affects the brain – particularly memory and cognition – were made in the Rockefeller University lab of the neuroendocrinologist Bruce McEwen. In the mid-1990s, McEwen and colleagues subjected adult rats to 'restraint stress', cramming them into cylinders resembling miniaturised iron lungs for six hours a day over the course of thee weeks. For the rats,

this was pretty much the same as a shot of rat-cortisol to the brain: stress induced by isolation and restraint withered the dendrites (the connecting structures responsible for communication between neurons) in the hippocampus, a seat of memory.

In another experiment, stressed rats and calm rats were set adrift in a watery eight-armed maze, with a peanut at the end of every arm. The stressed-out rats were less deft at recalling the location of the food, leading researchers to conclude that stress impaired their spatial memory. There was another twist: in the youngest animals, shrinkage of the dendrites reversed when stress abated. In middle-aged animals, the reversal was just partial, and in the oldest animals, there was no evident reversal at all. Shrivelled dendrites in the hippocampus, McEwen points out, have also been observed in humans suffering from dementia, chronic depression, schizophrenia and PTSD.

Recent findings suggest that chronic stress can lay down intransigent memories as well – especially those associated with aggression, violence or fear. In a 2005 study, McEwen compared young adult rats stuffed into airless plastic bags two hours a day for 10 days to counterparts stuffed into the bags for two hours, just once. Afterwards, under the microscope, the brains of the chronically stressed-out individuals had bushy nerve branches snaking around the amygdala, a corner of the brain that forms long-lasting fear memories.

Human loneliness, however unremitting, can’t be replicated by a rat squeezed into a plastic bag. But McEwen says the effect is evolutionarily conserved. In the face of isolation, measures of brain function and neuroimaging should show the same abnormalities, no matter what the species involved. McEwen says these irregularities are likely to cluster in a number of places. The hippocampus – where memories, including spatial memories, are stored – is likely to be diminished in size. The amygdala – which perceives threats and records fearful memories – is likely to get bigger and more hyperactive as it drives states of anxiety and depression. Meanwhile, the prefrontal cortex – which controls activity in the amygdala, as well as heartbeat, behaviour, and aggressive impulses – might lose neural cells and dwindle in size.

Hundreds of human studies show that even mild isolation can be a high-speed motorway to poor health – worse immunity, worse sleep, worse inflammation in the young, and higher rates of hypertension and cardiovascular trouble among the old. In 2002, epidemiologists at University College London studied 240 middle-aged civil servants and found that lonelier people had stress-associated increases in blood proteins and white blood cells that put them at higher risk for narrowed arteries, strokes, and hypertension. In 2012, a team of biochemists and gerontologists in Dublin measured both loneliness and blood glucose levels in 466 elderly people; the loneliest had the highest blood sugar levels, and a propensity to obesity and Type-2 diabetes.

Other studies connect social isolation with neuropsychiatric ills. In 2007, neurologists at Rush University in Chicago studied 823 elderly people and found a connection between loneliness and cognitive decline: the risk of Alzheimer's disease more than doubled among the loneliest of the group. In several experiments, psychologists studied isolation resulting from social rejection in teens. The excluded were more aggressive, less willing to exercise self-control, and had diminished cognitive abilities in tasks that required recollection and use of complex information.

Isolation puts prisoners at risk of anxiety, panic, chronic depression, rage, loss of control, paranoia, hallucinations, self-mutilation

Craig Haney, one of the leading correctional psychologists in the US, has testified to the psychological impact of solitary confinement on prisoners numerous times, including in the 2012 Senate hearing in Washington DC. In the course of his work over two decades, Haney has found that isolation puts prisoners at risk of a range of adverse symptoms: appetite and sleep disturbances, withdrawal, hypersensitivity, anxiety, panic, chronic tiredness and depression, rage, loss of control, paranoia, hallucinations, self-mutilation, and suicidal ideation and behaviour.

Yet existing research, including Haney's own study of 100 prisoners in isolation in California's Pelican Bay, have been constrained by 'ethical, legal, and practical barriers'. A truly randomised controlled study is nearly impossible to recreate in the context of a prison, because only a troop of white-coat Caligulas would feel

comfortable arbitrarily assigning some participants to solitary and some to the general population. On the rare occasion in 2010 that a prison granted access to researchers, the resulting study drew an unlikely conclusion: inmates actually appeared to get better during a one-year stint in solitary, at least initially.

Funded by the Department of Justice, and conducted by Maureen O'Keefe, the lead research director at the Colorado Department of Corrections, the study set out to assess how 270 prisoners fared over a year in Colorado State Penitentiary, a supermax in Cañon City. The first assessment was made, by self-report, when the inmates were held in temporary segregation after they'd being charged with breaking prison rules, and had faced an internal hearing to decide whether they'd be assigned to segregation. Some of them returned to the general population, some were sent to a facility for prisoners with psychiatric conditions, and others wound up in isolation. Over the rest of the year, prisoners from all three groups responded to questionnaires about their psychological states five more times. The conclusion was that all three groups improved at first, but then coasted without change to the end.

Haney, Kupers and Grassian denounced the study for pandering to the interests of the correctional authorities, but the study's authors and advisers are quick to point out its limitations as well: inmates were initially assessed during a tumultuous time, when they'd fought with someone, or had been attacked – which made for an unnaturally elevated baseline. The prison didn't have protective custody at the time of the study, so some inmates, rather than feeling oppressed, might have been relieved about being inaccessible to would-be assailants. And though hardly a resort, the prison was better serviced than some other facilities, since its inmates had a TV and a 'STEP' programme that rewarded good behaviour with privileges, which might have fostered some hope, possibly even a sense of agency.

Jamie Fellner, a psychiatrist who works on criminal justice issues with Human Rights Watch and oversaw the study, told me: 'The atmosphere and culture of a prison has a lot to do with the impact. How many phone calls do you get, how long do you get, what do you think your chances are of staying out of solitary. That's something we

didn't address.' Joel Dvoskin, a psychologist also involved in the study, averred: 'It's one study, in one prison system, and each system is unique, so it's not clear how generalisable it is. One harmful or skilful shift commander can change the entire environment in a prison, including a segregation unit.'

In a strong rebuttal to the study published in the *Correctional Mental Health Report* in 2011, Grassian and Kupers point out that self-reports are an unreliable measure of prisoners' mental states, especially when they don't take into account inmates' prior mental health history, and aren't backed by clinical reports. Not only do self-reports call for lucidity and self-awareness, which might be diminished among prisoners with mental health conditions, but they can be believed only if prisoners are safe from potential repercussions affecting future parole hearings or their prospects of being released from solitary.

Grassian and Kupers cite a specific example associated with the study itself. In 2008, an inmate enrolled in the study committed suicide despite the fact that, just prior to the incident, his self-report recorded no signs of distress. Kupers and Grassian insist that the study disregarded evidence of the prison's toxicity, including 37 emergency psychiatric contact reports for inmates in solitary during the course of the study compared with just three such reports among inmates in the general population.

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The larger problem, Haney told me, is that the most toxic solitary cells remain out of bounds for researchers, and that any brain scans to prove a link between solitary and brain damage would, in this context, be a fanciful prospect. 'Absent a judge telling a prison system that it "must" allow access by outside experts, few are willing to grant it, even for the purpose of interviews,' said Haney, who obtained most of his access through court orders. Just as with the Colorado study, the nature of that access has opened the impartiality of his work to question as well.

Complete answers will come only when more empirical research can be done. That might be a long way off, for all the reasons Haney suggests. But another set of Boxes is already being reformed, on the knowledge we have in our hands today. About nine months ago, Alex Dranovsky, a neuroscientist at Columbia who studies isolation and its effect on the brain, was surprised to hear that his university's Animal Care and Use Committee had amended its guidelines, and now forbade researchers from keeping animals alone in cages unless isolation was specifically part of the experimental design. This is in addition to rigorous scrutiny that review committees pay to the animals before every experiment, and periodic laboratory inspections. 'Well, I guess isolation is the cruellest thing we do to animals right now,' Dranovsky told me.

Meanwhile, every year, thousands of inmates leave solitary cells to join the ranks of parolees outside prison, their minds altered by an experience so fraught with risk that scientists require special dispensation to do it to animals.

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