WHAT WE **CAN LEARN** FROM **SYNAESTHESIA**

By Lily Dayton

Synaesthesia is a neurological phenomenon where a stimulus to one sense, like touch, also elicits a response in another sense, for example colour. As neurologists begin to unravel the mystery of these cross-sensory perceptions, they are discovering an in-road to understanding perception in general.

Like many people, some of Joel Salinas's earliest childhood memories involve a crayon box. But Salinas didn't simply draw pictures with the crayons inside – he interacted with each crayon on a personal level. "Each crayon had an emotion and a personality based on its colour," says Salinas, today chief resident for the Harvard Neurology Residency Program in Boston. "If I couldn't find a crayon in the box, I'd think it was because I'd hurt its feelings and it was pouting." To Salinas, the world is coloured in a spectrum of feelings, emotions, and personality traits. He associates numbers with particular colours – and the personalities of the colours also transfer to them. Even sounds and motions evoke the perception of colour. Salinas also ascribes colours and numbers to people he encounters.

It wasn't until Salinas was in medical school that he realized he perceived the world in an extraordinary way. While listening to a woman give a talk about the health benefits of meditation, a fellow student with a PhD in neuroscience commented that people who hear colours and see sounds can more easily reach a meditative state. Salinas recollects asking his friend later that night, "What do you mean? Doesn't everyone see colours with sound?" That's when he learned that he had a rare, inherited condition known as synaesthesia. Derived from Greek roots meaning "joined sensation", synaesthesia is a neurological phenomenon where a stimulus to one sensory modality kindles a percept in another sensory modality. To a synaesthete, these intersensory perceptions are immediate and automatic. But within the synaesthetic brain, there is an unusual cross-wiring of neuronal traffic, where normally separate brain areas are connected by sensory highways.

The number of sensory combinations that different synaesthetes describe is virtually unlimited – to some people, spoken words elicit different tastes on the tongue; to others, a texture on the fingertips may evoke a particular emotion. Overall, about 4% of the population experiences synaesthesia, with the most common form being coloured days of the week, followed by grapheme–colour synaesthesia, where people "see" each grapheme (letter or number) in a distinct colour. As neurologists begin to unravel the mystery of these cross-sensory perceptions, they are discovering an in-road to understanding perception in general.

Vilayanur Ramachandran, professor of neuroscience at the University of California at San Diego, was studying the phenomenon of phantom limbs in amputees in the early 1990s when he began to apply his findings to the nascent field of synaesthesia research. When Ramachandran touched the faces of people who had had their arm amputated, the amputees experienced a phantom sensation in their missing hand. "We found there was cross-wiring going on in the brain," says Ramachandran, explaining that within the somatosensory cortex, the part of the brain involved in tactile perception, lies a complete body map. The area corresponding to sensory input from the face is adjacent to the area for sensory input from the hand. Through magnetoencephalography, a technique that measures localized electrical activity in the brain, he validated a sensory re-mapping of brain areas. "If you remove →

Photo: Martin Klimas, o.T. (Paul Hindemith, "Ludus Tonalis") 2011

This alphabet shows how letters appear to the wife of graphic designer Jesse Jaren. For her, letters not only have a certain colour, but also a personality. This is a combination of grapheme–colour synesthesia and ordinal–linguistic personification. The full alphabet can be viewed in Jesse Jaren's blog "Cornfed in Seattle" (http://goo.gl/umHVNT).

the hand, no sensory input is going to the hand anymore, so the hand area hungers for sensory input. The face starts cross-activating the hand area. I started thinking about cross-activation in synaesthesia." Ramachandran and Edward Hubbard were the first to demonstrate that synaesthesia was a real perceptual phenomenon, rather than a memory association or fabrication. They devised a series of experiments in which they presented grapheme–colour synaesthetes and normal controls with a one-second view of a matrix of small black graphemes (for example, the letters P and F) in which additional graphemes (for example, the letter H) were arranged in a pattern that formed a geometrical shape, such as a triangle or square. To most people, the matrix would look like a jumble of small black letters. But to grapheme–colour synaesthetes, who perceived each grapheme in a distinct colour, the shape formed by the pattern of H-letters would "pop out" of the matrix and they could readily identify it. The researchers hypothesized that grapheme–colour synaesthesia arose from cross-activation between the areas of the brain that process graphemes and those that perceive colour. Today it's generally accepted that synaesthesia results from increased cross-talk between different brain areas, though there has been long-standing debate about whether this increased communication results from a structural increase in synaptic connections between brain regions or from diminished chemical inhibition that allows neurotransmission in one region to kindle excitation in another region.

Perhaps it's a bit of both, says Jamie Ward, professor of cognitive neuroscience at the University of Sussex. "It's been shown over the past few years that there are structural changes in the brain, but the question is how these differences develop. Synaesthesia could start as a chemical change that leads to a structural change."

In grapheme–colour synaesthetes, there are structural differences in parts of the brain involved in visual processing, such as the fusiform gyrus. But differences also extend to other regions of the brain that don't seem to be involved in either the visual processing of graphemes or colour. For example, compared with controls, grapheme–colour synaesthetes appear to have more grey matter on the lateral surface of the parietal lobes in a region called the intraparietal sulcus (IPS), an area thought to be involved with attention, working memory, and spatial representation of the external world. When grapheme–colour synaesthetes are presented with letters and numbers, they have greater fMRI activation in this region.

Comparison studies of grapheme–colour synaesthetes and non-synaesthetes show that grapheme–colour synaesthetes have a hyperactive visual cortex. If the visual cortex is stimulated with a magnet, synaesthetes show an enhanced EEG response and are more likely to report seeing visual imagery. Grapheme–colour synaesthetes are also better able to discriminate between high spatial frequency stimuli, such as textures with fine lines and colour gradations, says Nicolas Rothen, visiting research fellow at the University of Sussex. This gives them a memory advantage for words, abstract fractals, and geometric shapes (though not necessarily for autobiographical events). Recent research has shown brain differences in another kind of synaesthesia – mirror–touch synaesthesia, a condition in which a person observing touch to another person experiences a tactile sensation on the corresponding part of his or her body. "Functionally, when we observe people being touched, we all activate certain parts of our brain within the somatosensory cortex," says Michael Banissy, professor of psychology at Goldsmiths, University of London. "This is known as our mirror–touch system. When you show mirror–touch synaesthetes videos of people being touched, they activate the same system – but they have an overactive system."

Mirror–touch synaesthetes seem to have more grey matter in the somatosensory cortex, which is involved in empathy as well as touch perception. They also appear to have less grey matter volume at the temporal parietal junction, which is thought to be involved in the ability to distinguish between the self and others. Banissy explains that it may be because mirror–touch synaesthetes have an atypical self–other representation that they blur the boundaries between themselves and others.

When Salinas took part in a synaesthesia test in Ramachandran's lab, he was surprised to find out that he could add mirror–touch to the list of synaesthesia forms he experienced. "Up until that point, it was just part of my normal subjectivity," he says. He describes the feeling as being close to real, like a ghost of touch. Fortunately, he doesn't feel actual pain if he watches someone getting hurt – but he will feel a sensation. "It can certainly catch me off guard," he says. "I was doing a trauma rotation and I remember seeing someone's arm being amputated. I didn't feel pain, but I felt distressed. The thing that I felt most was the positioning of the hand and the parts that were macerated. It felt uncomfortable."

Just as grapheme–touch synaesthetes are more sensitive to certain visual stimuli, mirror–touch synaesthetes are more sensitive to tactile stimuli on their own bodies. "When we push little pressure pads with horizontal or vertical lines against their skin, mirror–touch synesthetes are better at discriminating the different textures," explains Ward. There is also evidence that mirror–touch synaesthetes are more socially sensitive than others. They are better able to recognize facial expressions and they rank high on measures of emotional empathy. Salinas says this skill helps him a great deal in his interactions with patients. "In certain situations with patients, I'm able to understand that they might be in distress, even if they're not really communicating that through words. I'll see their facial expression and pick up on their feelings because I'm feeling it in my body."

Another quality often associated with synaesthesia in general is creativity, and Ramachandran says there may be a link. "Synaesthesia is more common in poets, artists, and novelists. It may be that the hyperconnectivity [trait is] expressed more diffusely throughout their brains, which creates the propensity to connect brain regions and may create the propensity to be more creative." In a recent study, Rothen found the prevalence of synaesthesia among art students was 7%, which is higher than the 4% prevalence for the general population. "This suggests that either synaesthetes are more creative so they tend to study the arts, or their way of thinking in the arts helps to develop the synaesthetic experience …. The question is really what causes synaesthesia."

It's been known for over a century that synaesthesia tends to run in families, and 40% of synaesthetes report a family member who also has the condition. Yet inheritance patterns are elusive, with the trait often skipping a generation or occurring in a single family in a variety of different phenotypes. "A few years ago, people thought there was a single gene for synaesthesia," says Ward. "We currently believe there are several genes that convey susceptibility, maybe multiple genes, and the genes don't specify exactly what the outcome will be." →

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SYNAESTHESIA AND THE ARTS

Like many other artists, the Russian painter and art theorist Wassily Kandinsky is strongly suspected to have been a synaesthete who could hear colours and see music. He reports on a performance of Wagner's opera Lohengrin in Moscow: "I saw all my colours in spirit, before my eyes. Wild, almost crazy lines were sketched in front of me."

Katerina Kucera, postdoctoral researcher in the Language and Genetics Department at the Max Planck Institute for Psycholinguistics in Nijmegen, is taking two complementary approaches to searching for the genes involved in synaesthesia, in hopes that each will result in convergence on the same biological pathways. To look for the role of common genetic variants in synaesthesia, Kucera and colleagues are conducting an ongoing genome-wide association study: They are sampling DNA from a large number of unrelated synaesthetes to search for variants that are more common in synaesthetes than in the general population. Because they don't know if different types of synaesthesia share a common genetic mechanism, they are only looking at grapheme–colour synaesthetes in order to reduce genetic noise (information for potential participants can be found online at http://www.mpi.nl/synaesthesia). To look for rare genetic variants, Kucera is also currently working on an exome sequencing study, where she is sequencing the protein-encoding DNA sequences in three families with several members who have auditory–visual synaesthesia, in which sounds elicit visual experiences of colour and shape. "Right now we have some candidate variants that are shared by the synaesthetes in these families," she says, adding that they are currently validating whether the variants contribute to synaesthesia or whether they are simply shared because the family members are related. "Once we find the genes involved in synaesthesia, we will look at how variants alter proteins and the structure and function of neurons – and whether this has an effect on connectivity and signalling in the brain," says Kucera.

By learning about the physiological mechanisms and genetic underpinnings of synaesthesia, scientists are elucidating brain function in general. Isolating the genes for synaesthesia may give clues as to how genes influence brain networks – and what happens when brain circuitry goes awry. Atypical connectivity between brain regions has been implicated in a number of disorders, ranging from ADHD and autism spectrum disorder to schizophrenia, major depression, bipolar disorder, Alzheimer's disease, and post-traumatic stress disorder. Gaining an understanding of cross-talk within an otherwise healthy synaesthetic brain may someday lead researchers towards a cure for disorders that involve brain circuitry. But synaesthesia also offers a glimpse into different ways of thinking and being.

"For me, the interesting bit is using synaesthesia as a model to understand individual differences in perception," says Rothen. "Is your yellow the same as my yellow? Or is your yellow my blue? Or is it something different entirely? People understand the world in different ways. If we group them together – for example, synaesthetes and non-synaesthetes – we can begin to understand how individual differences in perception affect higher cognitive functions, such as memory and attention."

As a neurologist and a synaesthete, Salinas continues to be a scientific observer of his own life. Being constantly flooded with sensory stimulation can be overwhelming, so he's learned to experience his sensations – even uncomfortable ones – then process them and let them go. Salinas compares living with multiple forms of synaesthesia to "a practice of compulsory mindfulness." Empathizing with others and engaging with the people and objects he encounters on a multi-sensory level gives him the opportunity to be truly present with his world – and perhaps that's one thing we can all learn from synaesthesia.

Photo: Vassily Kandinsky/Composition 7/Wikimedia