Game of two halves leads to brain asymmetry

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A tug-of-war between the two sides of the brain causes it to become asymmetrical, according to research published today in the journal *Neuron*. Asymmetry in the brain is thought to be important to enable the two hemispheres to specialise and operate more efficiently.

Left-right asymmetry is present in the brains of most animals and is first evident at the time of early brain development. However, until now, scientists did not know the mechanisms that bring it about. Now, in a study funded primarily by the Wellcome Trust, researchers have shown that a competition between the two sides causes this asymmetry.

By studying brain development in zebrafish, PhD student Jenny Regan and her colleagues in Professor Stephen Wilson's team at UCL (University College London) have shown that a protein known as Fgf8 acts as a magnet to attract nerve cells to one side of the brain. .

"Fgf8 is found in both sides of the brain, leading to a 'tug-of-war' competition between the two sides to attract the migrating group of nerve cells," says Dr Regan. "This isn't a fair fight, however - Fgf8 on the left-hand side has an ally to help it win the battle."

A second protein, known as Nodal, is present only on the left and teams up with Fgf8 to attract the group of nerve cells, triggering a cascade of events that lead to asymmetric development of the brain, with neurons on the left making different connections to those on the right. The combined action of Fgf8 and Nodal ensures that when the asymmetry develops, it is usually in the same direction - this helps to explain why

there is consistent handedness between individuals. Nodal is known to also play a role in other areas of the body where asymmetry occurs, such as the heart and positioning of internal organs.

If Nodal is inhibited, the competition is fairer and the group of nerve cells has an equal probability of migrating to the right or left side, but a bias in the direction of migration can be restored by adding extra Fgf8 to one side of the brain.

"Brain asymmetry is essential for proper brain function," explains Professor Wilson. "It allows the two sides of the brain to become specialised, increasing its processing capacity and avoiding situations of conflict where both sides of the brain try to take charge.

"For example, faced with a predator, an animal would not want both sides of the brain to try to drive the escape as this might lead to conflict over which direction to turn. Instead, the animal might keep watch more with one eye (and consequently one half of the brain) and so each side of the brain might be dominant for particular activities."

Previous studies have shown that rearing chickens in the dark makes their brains less asymmetric. The chicks can still peck for food and watch out for predators, but only if doing one of these tasks at a time. When they try to do both, they are less efficient than fully asymmetric animals in which one eye specialises for one task and the other eye for the other task.

In humans, people with schizophrenia have disrupted brain asymmetries but as yet, it is not clear if there is a causal link between the asymmetry and schizophrenia.

"The direction and handedness that brain asymmetry takes is not critical for survival, but the strong bias towards one direction may be to ensure

that all members of a population have consistent behaviours," adds Professor Wilson. "This may be very important for social animals, such as humans and schooling fish."

Source: Wellcome Trust