Sox-less Mice Compulsively Groom

Psychiatric disorders are the mostly costly health issues facing western societies today and are often the most difficult for family and friends to cope with. Unlike many physical ailments, there is very little known about the mechanisms or heritable aspects of psychiatric disorders and this makes treatment through drugs and changes in life style very difficult to design. Fortunately, there is much work being done in this field and often results come from unexpected places.

Obsessive compulsive disorder (OCD) affects about two percent of the population and is one of the most common mental illnesses within any society. Since patients are obsessed by feelings of fear or incompleteness, they must compulsively or repeatedly act to subdue these. When a task in day to day life is performed, not only must our intentions (planned in the cortex) be translated into actions (organized within the striatum), but there must also be a feedback mechanism that confirms that the task has been completed (from the thalamus to the cortex). It has recently been shown that parts of the frontal cortex are underactive in clinical OCD cases, and if feedback within this network is not registered it is thought to produce feelings of anxiety, which must be satiated in some way. It is still unknown how the most widely used treatment for OCD, SSRIs (selective serotonin reuptake inhibitors), have their effect and if better treatments are to be developed, it is important that we gain a greater understanding of the physical networks involved in inducing obsessions and how compulsive action satisfies these.

Fortunately, researchers at the Karolinska Institute in Stockholm, Sweden, have found an interesting model for this disease quite by accident. Jonas Muhr's group works on the Sox family of proteins, and these are known for their role in pushing certain cells of a developing embryo towards being involved in the nervous system. Some Sox proteins have been shown to keep these 'neural' cells as progenitors, which can become several types of cells within the nervous system, while other Sox proteins have been shown to be involved in pushing progenitors towards becoming specific cell types. The group has previously published an article showing that the family member Sox21 is capable of making neural cells become brain cells, or neurons in science speak. Thus, they have recently produced a mouse that lacks the Sox21 gene and thus cannot make this particular protein during development. The published work suggested that these mice might have severe defects due to a hindered ability to produce neurons. However, the mice turned out to be born healthy and happy, with the single odd characteristic of grooming themselves too much. In fact, the mice have been seen to lick and groom themselves so compulsively that they pull out their fur.

This striking behaviour suggests that the defect within the Sox21 knockout mouse's brain may hold hints as to the developmental and neurological underpinnings of compulsive behaviour. Much work is left to be done; however, the researchers have narrowed down the defect to the developing cortex. The fact that the brains of the mutant adult mice show no obvious differences from those of their normal siblings suggests that the defect which leads them to over groom may be very subtle indeed. Much like human obsessive-compulsive disorder, it will be difficult to pin down exactly what is wrong with the brains of these mice. However, if the mental problems of these mice are shown to mirror those of clinical human cases of OCD, they could provide a very useful tool for both understanding and treating this complex disease.

Daniel Hagey
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Biology Education Centre, Uppsala University, and Ludwig Institute, Karolinska Institute. Supervisor: Jonas Muhr.