

Popular scientific summary – Neural differentiation of human embryonic stem cells

To date, research about human brain development has been based on animal studies, most commonly rodents such as rats and mice. These animal models are not suitable since the human brain is more complex and much bigger (the rat brain is 600 times smaller than the human brain and the mouse brain is 2000 times smaller). With a model of the early fetal brain made from stem cells it would be possible to perform more reliable studies as actual human cells are used. The effects of environmental chemicals on the fetal brain could be studied etc. Some chemicals might for instance be toxic resulting in cell death, whereas other chemicals could disturb the development of the fetal brain leading to neurodevelopmental disorders.

In order to address these unmet needs, a technical platform has been developed with the capability to generate a model of an early fetal brain structure known as the *neural tube*. The model is created from human embryonic stem cells which in a process known as *differentiation* can form any cell type found in the neural tube. By exposing stem cells to different local concentrations of a certain chemical substance, a so called *morphogen*, it is possible to direct them to differentiate into specific cell types, see **figure 1A**. Stem cells exposed to high concentrations of this morphogen form cell types found in a brain region called *hindbrain*. Cells that belong to another brain region called *midbrain* will be formed for intermediate concentrations while low concentrations yield cells in the *forebrain* region. The technical platform utilizes the relationship between morphogen concentration and cell type to form many different cell types simultaneously in each of the three brain regions, see **figure 1B**. Stem cells are initially cultured in a plastic dish. Then the technical platform is submerged into the plastic dish for differentiation of the stem cells. After 14 days of differentiation the device is removed and the three brain regions are generated.

