To carry out their study, Dr Muotri and his colleagues grew and examined hundreds of organoids, each a mere half-millimetre in diameter, over the course of ten months. To probe individual neurons within these they used tiny, fluid-filled pipettes that acted as electrodes small enough to maintain contact with the surface of an individual cell.

Neurons probed in this way proved electrically active, so the researchers went on to employ arrays of electrodes inserted simultaneously into different parts of an organoid to study its overall activity. They looked in detail, once a week, at each of the organoids that were chosen for examination. This revealed that, by six months of age, the electrical activity in different parts of an individual organoid had become synchronised.

Such synchronicity is also a feature of real brains, including those of preterm human infants of about the same age as Dr Muotri's organoids. It is regarded as an important part of healthy brain function. So, to check how similar natural and organoid brain waves actually are, the research team ran those waves obtained from their organoids through a computer program that had previously been trained to recognise the electrical activity generated by the brains of premature babies. This algorithm proved able to predict to within a week the ages of laboratory-grown organoids 28 or more weeks old. That suggests those organoids are indeed growing in a manner similar to natural human brains.

Brain work

If further research confirms this opinion, then for medical science that conformity with natural development could be a boon. Neuroscientists have long been held back by the differences between human brains and those of other animals—particularly the brains of rodents, the analogue most commonly employed in medical research. The purpose of the work that Dr Lancaster, Dr Muotri and others involved in the field are engaged in has always been to produce better laboratory models of neurological and psychiatric diseases, so that treatments may be developed.

And, although it may be some time in the future, there is also the possibility that organoids might one day be used as transplant material in people who have had part of their brains destroyed by strokes.

For ethicists, however, work like this raises important issues. A sub-millimetre piece of tissue, even one that displays synchronised electrical pulsing, is unlikely to have anything which a full-grown human being would recognise as consciousness. But if organoids grown from human stem cells start to get bigger than that, then the question that was posed back in 2013 becomes pressing. ■

Genetics and sexuality

There is no "gay gene"

But biology does in part determine sexual orientation

In 1993 a region of the human genome called xq28 was linked to male homosexuality, and the controversial notion of a "gay gene" was born. Those research findings have not been replicated. But it was never going to be that simple: decades of genetic research have shown that almost every human characteristic is a complex interplay of genes and environmental factors. A new study, published in *Science* this week, confirms that this is the case for human sexuality, too.

The study, the largest ever into this difficult topic, was conducted by an international group of scientists working with 23andMe, a personal genomics firm. It used what is called a genome-wide association study (GWAS) on 408,995 individuals in the UK Biobank, a British health resource, and 68,527 American 23andMe users—all of whom remained anonymous and consented to the study.

A GWAS involves scanning a person's DNA for tiny variations in the genetic code (simple changes in the As, Ts, Gs or Cs) that correlate with a given trait. The participants were divided on the basis of whether they answered yes or no to the question "Have you ever had sex with someone of the same sex?"—a woolly proxy for sexual orientation, even in the absence of little white lies. The figures the GWAS produced, therefore, relate only to a single act, not to whether someone identifies as gay.

The researchers found five genetic markers that were significantly associated with a reported homosexual act by one of the participants in the study. None of those markers was on the X or Y sex chromosomes and their total combined effect accounted for less than 1% of the variance. This is because the behaviour is the result of the aggregate effort of hundreds or thousands of genes, whose individual effects are infinitesimally weak. Totting up all the thousands of tested genetic variants accounted for between 8% and 25% of the variation in people's self-reported homosexual acts. These variants also overlapped with other traits, such as a smoking and an openness to new experiences.

Interestingly, only about 60% of the genetic variants identified in the study were shared by both sexes. Most behaviours show more overlap between the sexes than this, intimating that male and female homosexuality, or at least sexual adventures, may be quite different. David Curtis of University College London notes that what overlap there is "suggests that there could be specific factors affecting same-sex attraction rather than simply being attracted to males versus being attracted to females."

The riddles go on

Conscious of the tricky subject matter, the scientists are at pains to anticipate any misunderstandings or backlash. They collaborated with LGBT advocacy groups throughout the study.

Yet the research only scrapes the surface of the mysterious depths of human sexuality. Unravelling these riddles will be difficult and will inevitably beget misconception and controversy. But at least this study should add weight to the view that non-heterosexual behaviour is firmly within the normal, natural spectrum of human diversity and provide a firm foundation for future work. ■

Just part of the spectrum