Dorothy Bishop

Why I study...

Laterality

I MUST have been around four years old when I was first made aware that I was different. I was cheerfully colouring in a picture, when someone remarked, 'Oh, she's left-handed.' In general, my left-handedness was not much of an issue when I was a child. Teachers were tolerant, even though once I started to use ink, I had a habitual blue stain on my hand. Learning to knit – regarded as an essential skill for little girls at Downshall Primary – was rather a trial, but I'm not sure that my left-handedness was the principal obstacle.

It was when I started to read psychology at university that I realised that left-handedness might be a sign that my brain was organised differently from other people's. My excitement on discovering that left-handers were overrepresented among highly intelligent people, architects and musicians was tempered by finding that they were also prone to dyslexia, autism, stuttering, poor visuospatial skills, immune disorders and insomnia. More alarmingly, they were also at risk of early death.

It was easy to get lost in a field where, for each study that made a claim of an association with handedness, another study made a counterclaim. The one fact that people did seem to agree on was that most right-handers had left-hemisphere representation of speech, whereas for left-handers this association was much weaker, with around two thirds having left-hemisphere speech, and the remainder having either bilateral or right-hemisphere speech.

The strongest evidence for laterality in speech came from rates of aphasia after focal brain injury, which showed that persistent language problems after a left-hemisphere lesion were less common in left-handers than in right-handers. In intact humans, indirect evidence came from the methods I had first encountered in undergraduate practical classes: competing stimuli are presented to the two ears, or the two visual half-fields, typically leading to a small difference in favour of stimuli presented to one side or the other. The most dramatic evidence came from studies using the Wada technique to assess cerebral lateralisation in candidates for epilepsy surgery. This technique allows temporary anaesthesis of each hemisphere in turn to see whether this disrupts speech.

Having been led to an interest in cerebral lateralisation by my fascination with handedness, I became aware of even more fundamental questions. Why do humans have a lateralised brain? Towards the end of my undergraduate degree, I discovered the work of Marian Annett, and was impressed with the simple model she proposed to account for laterality differences between humans and other species.

Although there are some notable exceptions, in general, one does not see a population bias to one side or the other in handedness, or 'pawedness', in non-human animals. Individual animals may prefer the left or right side, but on average, the distribution of left- and right-siders will be 50:50. Annett plotted a hypothetical distribution of hand preference in non-human animals, and argued that the distribution for humans followed the same bell-shaped function, but this time with the mean shifted to the right. She proposed that humans have a 'right shift' gene, which evolved because it was important for cerebral lateralisation for language, and that superior skill of the right hand was an indirect consequence. The model was a probabilistic one: just as in animals, she suggested there are numerous environmental influences in the course of development that may push a person to prefer the left or right side. However, superimposed on these is the right shift factor.

Annett rejected any simplistic notion of genes for left- or right-handedness, but she argued that the right-shift gene was polymorphic – that is, it had different versions (alleles) in different people – hence there should be some family resemblance for handedness. Essentially, she argued that most people have two copies of the allele that favoured the left hemisphere and right hand (the rs+ allele).

Kate Grey

However, some people have a different version of the gene, which does not confer any advantage to either side. If a person has two copies of this rs– allele, then, except for a small influence of cultural factors, they have a 50:50 chance of being left- or right-brained. If they have two copies of the rs+ allele, they have a strong probability of being right-handed with left-hemisphere speech.

An immediate problem for Annett's theory is that, if the rs+ allele evolved to facilitate language lateralisation, and if language lateralisation is beneficial for humans, why hasn't the rs– allele disappeared by processes of natural selection? In general, polymorphic genes only persist in a population if there is no selective advantage for one allele over another. Annett suggested that people with the rs+– genotype have better reproductive fitness than those with two copies of either rs+ or rs–. Subsequently she carried out several studies attempting to test predictions from the model, by contrasting cognitive skills in different handedness groups. However, a convincing test is difficult to achieve, because we can only infer genotype very indirectly and imprecisely from measures of relative hand skill.

Opportunities to work on handedness waxed and waned after I completed my undergraduate degree. I completed clinical training at the Institute of Psychiatry in London (a mere two-year MPhil in those days), and went on to start my doctorate on neuropsychology of language in Oxford. A brief spell at the Montreal Neurological Institute provided the exciting opportunity to watch Wada testing in action.

While in Montreal, I decided that the time was ripe to do a comprehensive review of work on handedness and developmental disorder, and I began writing a book for the Clinics in Developmental Medicine series. I had great fun in libraries in Montreal and Oxford, poring over ancient and modern studies of handedness in rats, architects, parrots and members of remote African tribes. I came to the conclusion that the only developmental disorders that were reliably associated with atypical handedness were those in which there was evidence of organic brain impairment: epilepsy, severe learning disability and autism. The evidence for an association with specific reading disability seemed extremely weak.

'I told them I would eat my hat if they found anything'

My first serious study of handedness in children, carried out when I returned to Oxford, made me question whether one needed a genetic theory to account for the weak associations one could find between left-handedness and cognitive deficit. It was noteworthy that children with cognitive deficits were slightly more likely than other children to be left-handed, but this was related to poor right-hand skills. A non-genetic account of the association could be proposed whereby cognitive deficit was linked to mild damage to the motor system, perhaps caused by birth injury.

My current stance on the genetics of handedness is one of considerable scepticism. I think genes are involved in handedness, in so far as I think there is a gene (or genes) that differentiates humans from other animals. However, I'm not convinced there is genetic polymorphism for handedness. I was heavily influenced by a talk I heard on this topic by Kevin Laland. Just like Annett, he argued that all humans have a genetic bias toward right-handedness, but he did not regard the gene as polymorphic. Everyone has the same version, but environmental influences mean that the gene's influence is probabilistic rather than deterministic. Thus, individual differences in handedness are not seen as caused by genetic differences between people.

A couple of years ago I had the opportunity to look at the genetics of handedness more directly by analysing data from a twin study, where I had measures of hand preference and Annett's pegmoving task. As Laland would predict, there was no evidence of any genetic effect on either measure. Similarities between parents and offspring were entirely explicable in terms of cultural influence. However, shortly after I published this result, my colleagues at the Wellcome Centre for Human Genetics in Oxford started looking for genetic linkage with handedness. I told them I would eat my hat if they found anything. They not only found a linkage to chromosome 2, but having replicated this finding in a fresh sample they e-mailed me offering to provide a hat. So the jury is still out.

Handedness will continue to fascinate me for many years to come. It is a topic that raises particular methodological problems. It can seem deceptively easy to study – one can just send out a questionnaire without the need for detailed measurement. However, I think we need to strengthen the conceptual basis of our handedness measures if we are to get meaningful and replicable findings, bearing in mind the fact that hand preference and hand skill can be influenced by experience of writing and other skilled activities, as well as being subject to cultural pressures. We now have available far more sophisticated methods of brain imaging for assessing laterality of language functions directly in intact human beings, and these would seem the way forward when trying to account for associations with developmental disorders.

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