MICHELE THOMPSON

The orchid children

Are you a sensitive flower or a hardier type? It may all be down to an intriguing set of genes, as **David Dobbs** finds out

WHY are some children better at sharing than others? One attempt to find out uses what you could call the "Bamba test". In a large, playroom-like lab, a 3-year-old spends an hour or so playing games with a friendly woman, before snack time is announced. The adult brings out two packs of Bambas – peanut-butter-flavoured corn puffs much coveted in this part of the world.

The child's pack, like every normal one, holds 24 of the treats. But when the woman opens hers, she dumps out the contents and cries: "Mine has only three!" Will the 3-year-old share without being asked?

Most do not. "Self-initiated sharing is difficult," says psychologist Arial Knafo, who runs this study at The Hebrew University of Jerusalem in Israel. "You have to detect the need, then decide to do it."

A few 3-year-olds, however, will offer up their Bambas. What's different about them? The children most likely to share carried a certain gene variant, the "7R" version of *DRD4*, a gene that affects levels of the important brain chemical dopamine.

What made this finding remarkable was that this gene variant has generally been tied to *antisocial* behaviour. A pile of previous studies found that children with the 7R variant were more likely to be naughty and hyperactive. It had been dubbed the ADHD gene, the brat gene, the drinking gene, even the slut gene. Now Knafo was effectively calling it the Bamba-sharing gene. The bad-news gene was having a good effect.

This apparently paradoxical result lies at the heart of a major revision taking place in behavioural science – a recasting of the "vulnerability gene" model of many mood and behavioural disorders. This model, tremendously influential in psychiatry and psychology, has arisen over the past couple of decades as research tied several gene variants to high risk of mood and behavioural troubles, such as depression, aggression or, in the case of *DRD4*, attention and conduct disorders.

Crucially, these genes only caused problems when combined with a difficult childhood. Often termed vulnerability (or risk) genes, they have been held up as a prime model of how genes interact with environment to affect mood and behaviour.

But might we have got these genes all wrong? A fresh look at the evidence is suggesting that in fact they often create greater strength and happiness in people who have fortunate childhoods. The so-called vulnerability genes, in short, make you more attuned and responsive to your environment, whether bad or good.

"These genes aren't about risk," says Jay Belsky, a psychologist at the University of California, Davis, who helped establish what is being called the plasticity gene hypothesis, among other terms. "It is responsiveness – for better or worse."

The genetics of behaviour has always been a controversial field, with far-reaching implications for individuals and society. The origins of the vulnerability gene model lie in a study published in 1996 that showed we have a greater risk of becoming depressed or anxious if we have a certain version of a gene called *SERT*. The short version of this gene, which is carried by 30 to 50 per cent of people, lowers levels of serotonin, another brain chemical.

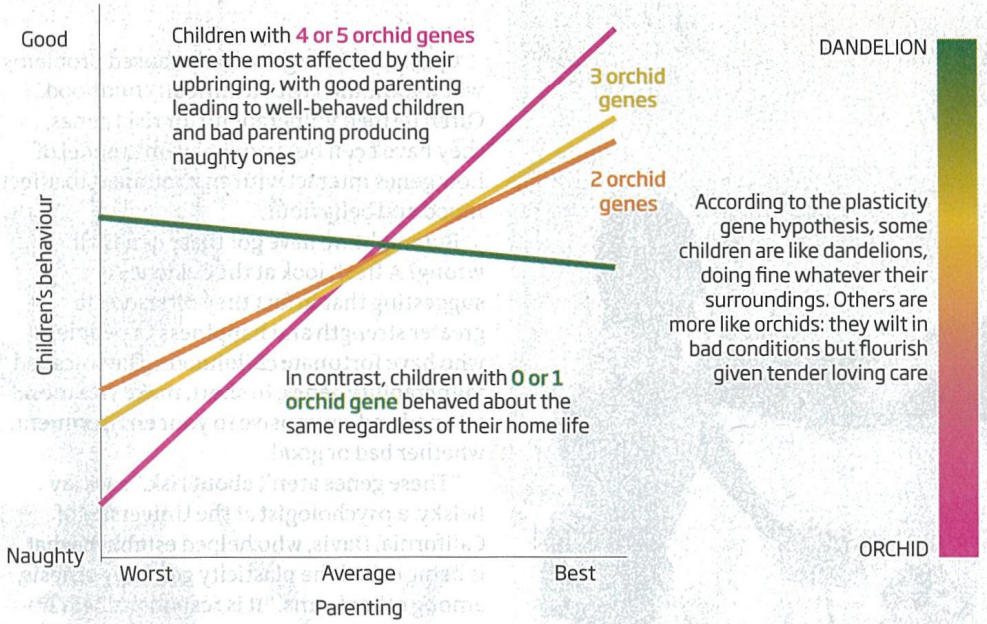
Serotonin was already much on the minds of psychiatrists and drug companies. The introduction of Prozac had created a growing class of antidepressants, called selective serotonin re-uptake inhibitors (SSRIs), thought to work by raising serotonin levels. The short version of *SERT* was quickly dubbed "the depression gene". Yet that label had to be too simplistic. A short *SERT* does not guarantee depression, it only raises the risk. Environmental factors also had to play a role.

That crucial mingling of nature and nurture seemed to be neatly elucidated a few years later by two seminal studies from epidemiologists Avshalom Caspi and Terrie Moffitt of King's College, London. They found that a short *SERT* raised people's risk of depression only if they suffered rough childhoods or episodes of intense stress as adults (*Science*, vol 301, p 386). They also showed that a variant of a gene called *MAOA*, which affects serotonin and several other brain chemicals, increased the chance of violent or sociopathic behaviour, but only in people who were abused as children (*Science*, vol 297, p 851).

The two papers attracted enormous attention and spurred many further studies. While not all replicated Caspi and Moffitt's results, many did, and so the vulnerability ›

Nature and nurture

The effects of parenting on children's behaviour depends on how many "orchid" genes they carry



SOURCE: JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY (VOL 52, P 619)

gene model came to dominate the field of behavioural genetics.

But not everyone was buying it. Back in 1995, W. Thomas Boyce, a child development specialist then at the University of California, Berkeley, had been trying to understand why some children seemed to react more to their environment in measures ranging from heartbeat and blood pressure to levels of cortisol, a hormone related to stress. Boyce examined how this reactivity affected rates of asthma in children aged 3 to 5. While some had the same rates of illness regardless of their home life, more reactive kids had worse asthma if they lived in stressful environments and less asthma if in low-stress homes. They were simply more sensitive to their environment, whether bad or good.

Upside ignored

Boyce was soon joined in this line of inquiry by Bruce Ellis at the University of Arizona in Tucson. Together they speculated that this reactivity also affects mood and behaviour. Drawing on Swedish terms, they distinguished between "dandelion children", who did about the same whatever their environment, and "orchid children", who wilted under poor care but flourished if carefully tended (*Development and Psychopathology*, vol 17, p 271).

Then, in 1997, Belsky also raised the idea of children who were especially sensitive to their early environments. Initially unaware of Boyce and Ellis's work, he was trying to figure out why some troubled kids responded more than others to counselling or other interventions to change their behaviour.

As Belsky, Boyce and Ellis watched the vulnerability-gene studies accumulate, they realised these could be the very genes that prompted the sensitivity they had found. And when Belsky delved into the literature he found evidence showing exactly that. Many vulnerability-gene studies indeed seemed to show that the so-called bad variants of *SERT*, *DRD4*, and *MAOA* generated extra resilience and other assets in people with fortunate early years. Yet the literature largely ignored this upside: in paper after paper, the raw data and graphs indicated the positive effects, but the text failed to explore or even note them.

Belsky was quite happy to note them. In 2006, he and others began publishing new studies and re-analyses of old ones showing that the so-called vulnerability genes created not just risk but bidirectional sensitivity.

Other groups started to investigate the idea. Knafo, for instance, began exploring *DRD4*'s effect on social behaviour, as described earlier. He has shown that as long as parenting is good, toddlers with the 7R variant are more "prosocial" than those with the more common 4R form (*Development and Psychopathology*, vol 23, p 53). The orchids not only shared their Bambas, but were also more likely to pick up a researcher's dropped pencil, express sympathy over a bumped knee, and help find and then comfort a lost doll.

Knafo found that this edge in sociability and generosity increased over the three years he followed the children. This may simply reflect the natural course of child development. Or it may reflect a positive feedback loop, as both responsive child and engaged parent react to their good chemistry. Some of the mothers probably carry the 7R variant too, since a 7R child must have at least one 7R parent. Knafo hadn't genotyped them, so he can't say.

In 2008, another team showed that *DRD4*'s 7R variant does not just make its bearers more responsive to natural variations in their upbringing; those carrying it also respond more to experimental interventions. In a programme for mothers of difficult toddlers that trained them to be more engaged and attentive, children carrying the 7R variant benefited the most (*Developmental Psychology*, vol 44, p 293).

Belsky, meanwhile, is doing bigger studies that gauge the cumulative effects of several plasticity genes. In 2010, he published an analysis drawn from a 12-year study of 1586 adolescents. He analysed five genes (*SERT*, *MAOA*, *DRD4*, and two other genes that regulate dopamine) and collected data on the teens' behaviour and self-control, and on the mothers' engagement in their lives.

The numbers, once crunched, showed no significant effects on girls. But the 754 boys did react differently according to their genes, showing distinct dandelion or orchid effects (*Journal of Child Psychology and Psychiatry*, vol 52, p 619). The boys with no or only one plasticity variant proved to be dandelions: they fared about the same regardless of how engaged their mothers were. Those with two to five plasticity variants, however, responded like orchids, and the more they had, the more sensitive they were (see diagram, left).

With the caveat that this kind of multiple-gene study has not yet been replicated, the effect found seems to fit the orchid hypothesis

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"The restlessness and risk-taking we call ADHD may have helped drive human expansion out of Africa"

beautifully. It also accords with the principle that complex traits are generally determined by many genes, not just one.

In addition, the lack of effect in boys with just one plasticity variant offers an explanation for a puzzle hanging over the field for years: the failure of some single-gene studies to show the expected effects. Belsky's research suggests that the effect of any one gene depends on the others.

Support is coming from other fields as well. Orchid-dandelion effects have been found in rhesus monkeys, the only primate besides humans to have the short *SERT* variant. Ethologist Stephen Suomi of the US National Institutes of Health in Bethesda, Maryland, has done experiments with these monkeys that cannot be done with people, such as swapping babies at birth to switch the kind of parenting they receive. Unlike dandelion monkeys, orchid monkeys tend to turn out neurotic if raised by insecure, neurotic mothers but resilient and self-assured if raised by secure, competent mothers.

The orchid hypothesis also meshes with observations of adults in psychotherapy. Since 1997, Californian psychiatrists Elaine and Arthur Aron have written about what they call "highly sensitive persons", or HSPs, who are especially responsive not just to trouble but to many of life's pleasures and subtleties. As Elaine Aron sees it, this group, comprising an estimated 15 to 20 per cent of the population, perceive life at a finer, more nuanced scale.

As the plasticity theory gained ground, the Arons and others have wondered if HSPs are essentially orchid children grown up. They argue that HSPs share with the orchid children a particularly reactive physiological and sensory response to the world.

Now the first genetic evidence is emerging to support that view. One set of preliminary results, presented at last year's annual meeting of the US Society of Biological Psychiatry in San Francisco, found that HSPs were more likely to carry the short *SERT* gene (see bit.ly/thFP3i). Another, also published in 2011, correlated HSP characteristics with 10 genetic variations that affect dopamine levels (*PloS One*, vol 6, p e21636).

Evolutionary asset

All this work from different fields has given the plasticity hypothesis far more traction in the past two to three years. "This thing is just exploding," as Belsky puts it.

The idea is taking hold fastest among specialists in child development. At the 2009 biennial meeting of the Society for Research in Child Development, the plasticity hypothesis was mentioned only in passing. At the subsequent meeting, in 2011, it was the main subject of half a dozen sessions. Meanwhile, the February 2011 issue of *Development and Psychopathology* carried a special section with a dozen papers on it (vol 23, p 1).

The plasticity hypothesis is also gaining ground in fields such as adult psychology, behavioural genetics and anthropology. Five years ago you could count on your fingers the researchers doing this work, says Belsky. Now dozens have written papers, which "come out so fast now, that when I write review papers, the review is outdated before it's printed".

Another telling sign came in 2010, when the originator of the vulnerability-gene hypothesis was converted. Klaus-Peter Lesch, a psychiatrist at the University of Würzburg in Germany, who discovered the short *SERT* gene in 1995, wrote a paper titled "Looking on the bright side of transporter gene variation". In it, he called for the short *SERT* to be seen as an evolutionary asset.

In fact, many of the orchid-theory supporters argue that even with its drawbacks, sensitivity is more often than not adaptive – and therefore selected for. This idea has gained credence by the discovery over the last decade that many of the plasticity genes have spread rapidly through humankind over the last 50,000 years.

Of the leading orchid-gene variants – the short *SERT*, the 7R *DRD4* and the more plastic version of *MAOA* – none existed in humans 80,000 years ago. Since emerging, these variants have spread into 20 to 50 per cent of the population. "That's not random drift," says John Hawks, an evolutionary anthropologist at the University of Wisconsin-Madison. "They're being selected for."

Orchid genes could provide an advantage in several ways. To start with, they seem to create better mental health and greater resilience in people with secure, stimulating childhoods. The "problem" traits they can generate, such as anxiety, aggression or ADHD, could help survival in conflict-ridden or volatile environments. Plasticity genes also boost resilience at the group level by creating a mix of steady do-ers (dandelions) and individuals with greater behavioural range (orchids).

Some evolutionary anthropologists argue that these traits, particularly the restlessness and risk-taking found in many carriers of the 7R *DRD4*, may have helped drive human expansion. Today the 7R variant is most common in populations that migrated fastest and furthest from Africa (*American Journal of Physical Anthropology*, vol 145, p 382).

It may seem odd to link such achievements to a child's willingness to share Bambas. Yet if the orchid hypothesis is right, the genes that help create some of our most grievous frailties – anxiety and aggression, melancholia and murder – may also underlie our greatest strengths, from the sharing of meals to our spread around the globe. Something to ponder next time you're offered a sweet. ■

David Dobbs is writing his fourth book, *The Orchid and the Dandelion*. You can find more of his writing at daviddobbs.net