1

Edible knowledge: the chemical transfer of memory

Introduction

Everyone is fascinated by memory and nearly everyone feels that they would prefer their memory to be a little better. Memorising lines in a play, or memorising multiplication tables, is the kind of hard work that people like to avoid. The slow growth of experience that counts as wisdom seems to be the gradual accumulation of memories over a lifetime. If only we could pass on our memories directly we could use our creative abilities from an early age without needing to spend years building the foundations first.

Between the late 1950s and the mid-1970s it began to look as though one day we might be able to build our memories without the usual effort. This was as a result of experiments done by James V. McConnell and, later, Georges Ungar, on the chemical transfer of memory in worms and rats. If memories are encoded in molecules then, in principle, it should be possible to transfer *The Complete Works of Shakespeare* to memory by ingesting a pill, to master the multiplication tables by injection into the bloodstream, or to become fluent in a foreign language by having it deposited under the skin; a whole new meaning would be given to the notion of 'swallowing the dictionary'. McConnell and Ungar believed they had shown that memories were stored in chemicals that could be transferred from animal to animal. They believed they had shown that substances corresponding to memories could be extracted from the brain of one creature and given to a second creature with beneficial effects. If the first creature had been trained in a task, such as turning left or right in an alley in order to reach food, the second creature would know how to reach the food without training – or, at least, with less than the usual amount of training. The second creature would have, as one might say, 'a head start', compared with one which had not had the benefit of the substance corresponding to the memory.

Worms

The first experiments were done by McConnell on planarian worms, a type of flatworm. McConnell trained them to scrunch up their bodies in response to light. He shone a bright light on the worms as they swam along the bottom of a trough, and then gave them a mild shock which caused their bodies to arch or 'scrunch'. Eventually the worms learned to associate light with shock and began to scrunch when a light was shone upon them whether or not the shock was delivered. Worms that scrunched in response to light alone counted as 'trained' worms. This is how McConnell described the experiments

> Imagine a trough gouged out of plastic, 12 inches in length, semi-circular in cross-section, and filled with pond water. At either end are brass electrodes attached to a power source. Above the trough are two electric light bulbs. Back and forth in the trough crawls a single flatworm, and in front of the apparatus sits the experimenter, his eye on the worm, his hands on two switches. When the worm is gliding smoothly in a straight line on the bottom of the trough, the experimenter turns on the lights for 3 seconds. After the light has been on for two of the three seconds, the experimenter adds one second of electric shock, which passes through the water and causes the worm to contract. The experimenter records the behaviour of the worm during the two-second period after the light has come on but before the shock has started. If the animal gives a noticeable turning movement or a contraction prior to the onset to the shock this is scored as a 'correct' or 'conditioned' response. *(McConnell, 1962, p.42)*

Now this sounds fairly straightforward but it is necessary to go into detail from the very beginning. Planarian worms scrunch their bodies and turn their heads from time to time even if they are left alone. They will also scrunch in response to many stimuli, including bright light. To train the worms, McConnell had first to discover the level of light that was bright enough for the worms to sense, but not so bright as to cause them to scrunch without the electric shock. Since worm behaviour varies from time to time and from worm to worm we are immediately into statistics rather than unambiguous yes's and no's. What is worse, the effectiveness of the shock training depends upon the worm not being scrunched when the shock is delivered. A worm that is already scrunched has no response left to make to light and shock, and therefore experiences no increment in its training regime when the stimulus is administered. It turns out, then, that to train worms well, it is necessary to watch them carefully and deliver the stimuli only when they are swimming calmly. All these aspects of worm training require skill – skill that McConnell and his assistants built up slowly over a period. When McConnell began his experiments in the 1950s he found that if he trained worms with 150 'pairings' of light followed by shock it resulted in a 45% scrunch response rate to light alone. In the 1960s, by which time he and his associates had become much more practised, the same number of pairings produced a 90% response rate.

In the mid-1950s McConnell tried cutting trained worms in half. The planarian worm can regenerate into a whole worm from either half of a dissected specimen. McConnell was interested in whether worms that regenerated from the front half, containing the putative brain, would retain the training. They did, but the real surprise was that worms regenerated from the brain-less rear half did at least as well if not better. This suggested that the training was somehow distributed throughout the worm, rather than being localised in the brain. The idea emerged that the training might be stored chemically.

McConnell tried to transfer training by grafting parts of trained worms to untrained specimens, but these experiments met with little success. Some planarian worms are cannibalistic. McConnell next tried feeding minced portions of trained worms to their naive brothers and sisters and found that those who had ingested trained meat were about one-and-a-half times more likely to respond to light alone than they otherwise would be. These experiments were being reported around 1962. By now, the notion that memory could be *transferred* by chemical means was the driving force of the experiments.

Arguments about the worm experiments

Transplantation versus chemical transfer

The notion that training or memory could be transferred by chemical means gave rise to substantial controversy. One counter argument was to agree that training was being transferred between worm and worm but to argue that it had no great significance. The planarian worm has a digestive system that is quite different from that of a mammal. The worm's digestive system does not break down its food into small chemical components but rather incorporates large components of ingested material into its body. To speak loosely, it might be that the naive worms were being given 'implants' of trained worm – either bits of brain, or some other kind of distributed memory structure – rather than absorbing memory substance. This would be interesting but would not imply that memory was a chemical phenomenon and, in any case, would probably have no significance for our understanding of memory in mammals. McConnell's response to this was to concentrate on what he believed was the memory substance. Eventually he was injecting naive worms with RNA extracted from trained creatures, and claiming considerable success.

Sensitisation versus training

Another line of attack rested on the much more basic argument that planarian worms were too primitive to be trained. According to this line, McConnell had fooled himself into thinking that he had trained the worms to respond to light, whereas he had merely increased their general level of sensitivity to all stimuli. If anything was being transferred between worm and worm, it was a sensitising substance rather than something that carried a specific memory.

It is difficult to counter this argument because any kind of training regime is likely to increase sensitivity. Training is done by 'pairing' exposure to light with electric shock. One way of countering the sensitisation hypothesis is to subject the worms to the same number of shocks and bursts of light, but in randomised order. If sensitisation is the main effect, then worms subjected to a randomised pattern of shocks and light bursts should be just as likely to scrunch in response to light alone as worms subjected to properly organised pairings of stimuli. If it is training rather than sensitisation that is important, the trained worms will do better.

Once more, this sounds simple. Indeed, McConnell and other 'worm runners' did find a significant difference between *trained* and *sensitised* worms, but the effect is difficult to repeat because training is a matter of *skilled practice*. As explained above, to effect good training it is necessary to observe the worms closely and learn to understand when they are calm enough for a shock to produce a training increment. Different trainers may obtain widely differing outcomes from training regimes however much they try to repeat the experiments according to the specification.

To the critic, the claim that a poor result is the outcome of poor training technique – specifically, a failure to understand the worms – sounds like an *ad hoc* excuse. To say that only certain technicians understand the worms well enough to be able to get a result sounds like a most unscientific argument. Critics always think that the claim that only some people are able to get results – the 'golden hands' argument, as one might call it – is *prima facie* evidence that something unsound is going on. And there are many cases in the history of science where a supposedly golden-handed experimenter has turned out to be a fraud. Nevertheless, the existence of specially skilful experimenters – the one person in a lab who can successfully manage an extraction or a delicate measurement – is also widely attested. In the field of pharmacology, for example, the 'bioassay' is widely used. In a bioassay, the existence and quantity of a drug is determined by its effects on living matter or whole organisms. In a sense, the measurement of the effect of various brain extracts on worms and rats could be seen as itself a bioassay rather than a transfer experiment. Yet the bioassay is a technique that has the reputation of being potentially difficult to 'transfer' from one group of scientists to another because it requires so much skill and practice. It is, then, very hard to separate golden hands from *ad hocery*, a problem that has a particular salience in this field. Certainly attributions of dishonesty are not always appropriate.

For this kind of reason the argument between McConnell and his critics was able to drag on, reaching its zenith in 1964 with the publication of a special supplement to the journal, *Animal Behaviour*, devoted to the controversy. At this point it would be hard to say who was winning, but it was clear that McConnell's claim that training worms required special skills was becoming a little more acceptable.

Confounding variables and replication

Sensitisation could be looked at as a confounding variable, and critics put forward a number of others. For example, planarian worms produce slime as they slither along. Nervous worms prefer swimming into slimed areas which have been frequented by other worms. A naive worm swimming in a two-branched alley will naturally prefer to follow the path marked out most strongly by the slime of worms that have gone before. If the alley has been used for training, the preferred route will be that which the trainee worms have used most often. Thus, naive worms might prefer to follow their trained counterparts not because of the transfer of any substance, but because of the slime trails left before. Even in an individual worm it might be that the development of a preference for, say, right turns, might be the build-up of a self-reinforcing slime trail rather than a trained response.

Once this has been pointed out there are a number of remedies. For example, the troughs might be scrubbed between sessions (though it is never quite clear when enough scrubbing has been done), or new troughs might be regularly employed. One critic found that in properly cleaned troughs no learning effect could be discovered, but McConnell, as a result of further research, claimed that worms could not be trained properly in a clean environment. He suggested that worms were unhappy in an environment made unfamiliar because it was free of slime; too much hygiene prevented the experiments working. One can readily imagine the nature of the argument between McConnell and his critics over the effects of sliming.

Eventually, this part of the argument was resolved, at least to McConnell's satisfaction, by pre-sliming training grounds with naive worms that were not part of the experiment. This made the troughs and alleys comfortable for the experimental subjects without reinforcing any particular behaviour.

All these arguments take time, and it is not always clear to everyone exactly what has been established at any point. This is one of the reasons why controversies drag on for so long when the logic of the experiments seems clear and simple. Remember, too, that every experiment requires a large number of trials and a statistical analysis. The levels of the final effects are usually low so it is not always clear just what has been proved.

Whether or not McConnell's results could be replicated by others, or could be said to be replicable, depended on common agreement about what were the important variables in the experiment. We have already discussed the necessity – from McConnell's point of view – of understanding and of skilled handling of the worms. In his own laboratory, the training of 'worm runners' by an experienced scientist was followed by weeks of practice. It was necessary to learn not to 'push the worms too hard'. In his own words:

> [it is necessary to] treat them tenderly, almost with love . . . it seems certain that the variability in success rate from one laboratory to another is due, at least in part, to differences in personality and past experience among the various investigators. *(McConnell, 1965, p.26).*

As explained, to look at it from the critics' point of view, this was one of the *excuses* McConnell used in the face of the palpable non-repeatability of his work. The effect of sliming was another variable cited by both proponents and critics in their different ways.

As a scientific controversy develops more variables that might affect the experiments come to the fore. For the proponents these are more reasons why the unpractised might have difficulty in making the experiments work; for the critics, they are more excuses that can be used when others fail to replicate the original findings.

In the case of the worm experiments up to 70 variables were cited at one time or another to account for discrepancies in experimental results. They included: the species and size of the worms; the way they were housed when not undergoing training – was it in the dark or the light?; the type of feeding; the frequency of training; the temperature and chemical composition of the water; the strength of the light, its colour and duration; the nature of the electric shock – its pulse shape, strength, polarity and so forth; the worm's feeding schedule; the season of the year; and the time of day when the worms were trained. Even the barometric pressure, the phase of the moon, and the orientation of the training trough with respect to the earth's magnetic field were cited at one time or another. This provided ample scope for accusation and counter-accusation – skill versus *ad hocery*. The greater the number of potential variables, the harder it is to decide whether one experiment really replicates the conditions of another.

The Worm Runner's Digest

McConnell was an unusual scientist. What people are prepared to believe is not just a function of what a scientist discovers but of the image of the work that he or she presents. McConnell was no respecter of scientific convention and in this he did himself no favours. Among his unconventional acts was founding, in 1959, a journal called *The Worm Runner's Digest*. He claimed this was a way of coping with the huge amount of mail that he received as a result of the initial work on worms, but the *Digest* also published cartoons and scientific spoofs.

Ironically, one of the disadvantages of the worm experiments was that they seemed so easy. It meant that many experimenters, including high school students, could try the transfer tests for themselves. It was these high school students who swamped McConnell with requests for information and accounts of their results. The newsletter, which became *The Worm Runner's Digest*, was McConnell's response.

It is not necessarily a good thing to have high school students repeat one's experiments for it makes them appear to lack *gravitas*. What is worse, it makes it even more difficult than usual to separate serious and competent scientific work from the slapdash or incompetent. It is certainly not a good thing to found a 'jokey' newsletter if you want your work to be taken seriously.

In 1967 the journal split into two halves, printed back to back, with the second half being re-titled *The Journal of Biological Psychology*. This journal was treated in a more conventional way, with articles being refereed. The idea was that the more serious work would appear in the refereed end of the journal while the jokey newsletter material would be reserved for the *Digest* half. (The analogy between the journal and the front and back halves of regenerating worms was not lost on McConnell and the contributors. Which end contained the brain?) *The Journal of Biological Psychology*, refereed though it was, never attained the full respectability of a conventional scientific outlet. How could it with *The Worm Runner's Digest* simultaneously showing its backside to scientific convention in every issue?

Because a number of McConnell's results were published in *The Worm Runner's Digest/The Journal of Biological Psychology* scientists did not know how to take them. To put it another way, any critic who was determined not to take McConnell's work seriously had a good excuse to ignore his claims if their only scientific outlet was in McConnell's own, less than fully attested, journal. In the competition between scientific claims, the manner of presentation is just as important as the content. The scientific community has its ceremonies and its peculiar heraldic traditions. The symbols may be different – Albert Einstein's unruly hair and Richard Feynman's Brooklyn accent in place of gilded lions and rampant unicorns – but the division between scientific propriety and eccentricity is firm if visible only to the enlightened. Much of what McConnell did fell on the wrong side of the line.

The ending of the worm controversy

Around the mid-1960s, as McConnell was beginning to establish that worms could be trained, if not that the transfer phenomenon could be demonstrated, the stakes were changed in such a way as to make some of the earlier arguments seem petty. This was the result of experiments suggesting that the transfer phenomenon could be found in mammals.

Some of McConnell's most trenchant critics had argued that planarian learning was impossible, others that it had not been fully proved. We may be sure that the strong attacks on learning were motivated by the importance of the transfer phenomenon. With the apparent demonstration of transfer in rats and mice, the objections to planarian learning dropped away. Rats and mice are familiar laboratory animals. There is no dispute that they can learn, and there is no dispute that in order to learn they have to be carefully handled. It is acknowledged that the technicians who handle the rats in a psychology or biology laboratory must be skilled at their job. Once the worm experiments were seen through the refracted light of the later experiments on rats it appeared entirely reasonable that worms should need special handling, and entirely reasonable that they could learn. The believers in McConnell's results stressed this, as in the following quotation from two experimenters:

> It seems paradoxical that when we run rats, we handle our subjects, we specify what breeding line the stock is from, we train them in sound-proof boxes, and we specify a large number of factors which when put together give us an output we call learning . . . Planarians on the other hand are popped into a trough, given a . . . [conditioned stimulus] and . . . [an unconditioned stimulus] and are expected to perform like a learning rat. *(Corning and Riccio, 1970, p.129).*

But this kind of *cri de coeur* only came to seem reasonable to the majority at a later date. It only became acceptable when nobody cared very much because their attention had been turned to the much more exciting subject of transfer of behaviour among mammals. This was a much more important challenge to received wisdom about the nature of memory.

Mammals

Early experiments

The first claims to have demonstrated memory transfer in mammals came from four independent groups working without knowledge of each other's research. The first four studies were associated with the