The future biology of happiness: lifestyle changes or recreational drugs?

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We have been on a long journey together considering how the brain controls behaviour in both man and other animals and why this can sometimes go wrong and lead to a wide variety of problems. At the heart of this journey has been the question of what makes man different from other species. We have seen that in many ways he is not so different although perhaps in one important aspect of behaviour he often seems remarkably difficult to please compared with other species and that concerns his happiness. Man it seems is often not as happy with his lot as he feels he should be and has increasing expectations of external influences such as science and governments to make improvements.

The science of happiness

In the last decade in particular the issue of what makes people happy, what we as individuals can do to help ourselves and what science and governments can do to help with this process has become a big deal. There is some confusion about what is being measured when one talks about happiness and thus we have a growing number of buzz words or phrases which try to capture its technical essence – “Sense of well-being”, “Good quality of life”, “Life satisfaction” etc. Indeed the question is not just being asked about humans but also domestic and companion animal species. In September this year there will be a two day series of talks held at the Royal Society called “Quality of Life: Heart of the Matter” organised by the Universities Federation of Animal Welfare and the British Veterinary Association where I will be talking about the impact of brain evolution (see www.ufaw.org.uk for conference details)

However, while all these various “well-being” parameters tend to be associated with happiness they do not necessarily equate to it.

In many ways happiness is more of a concept that an easily defined state. Many researchers seem to split happiness into different levels. At the basic level 1 there is a generally short term euphoric experience of joy and pleasures (“momentary feelings”) whereas at level 2 there is a more cognitive and longer term experience of satisfaction and contentment (judgement about feelings”). These are obviously not mutually exclusive. Daniel Nettle (2005) describes these in his recent book “Happiness the science behind your smile” and also defines a level 3 which he terms “quality of life” and includes feelings of flourishing and fulfilling one’s potential. Level 2 and 3 happiness are naturally somewhat harder to achieve if you have high expectations in life.

In most cases happiness is measured by using questionnaires that ask you questions about how you feel and react to various situations. They are similar to most personality type questionnaires. A more direct way is to measure brain activity in an MRI scanner or by making electrical recordings. Happy people show strong activation in their left prefrontal cortex whereas people experiencing negative emotions tend to have

stronger activation in the right prefrontal cortex. These areas are connected with an area important form the expression of emotion, the amygdala. I have mentioned in a previous lecture this idea of the happy left brain and sad right brain although it is unlikely to be quite as simple as this because the right side of the brain is involved with intense emotions of both positive and negative kinds and when you view people you are in love with! Hopefully you are happy when you see a picture of a loved one!

No matter how it is measured though, the importance of happiness in the political and economic arena is on the increase. This has been underlined by the explosion of books and statistics on the subject and the award of the Nobel prize for Economics in 2002 to a Psychologist studying what influences how people make judgements and the role of emotional factors such as happiness - Daniel Kahneman.

It is not my intention in this lecture however to focus entirely on the psychology of happiness. The Gresham visiting Professor of Psychiatry, Raj Persaud, has already done this recently in his lecture entitled “How to be Happy” in December 2005. There are also a number of recent books on the subject (Layard, 2005; Nettle, 2005; Seligman, 2003). Indeed, what is clear from twin studies is that 70-80% of what determines a happy personality is down to your genes and of the other 20-30% that is influenced by experience there is little doubt that a happy childhood plays a role, having good social and emotional support from friends and partners and having a job and financial security. Having a strong religious belief is also a contributory factor. However, it is emotional rather than material factors that tend to play the major role in developed countries with earnings contributing relatively little after a basic level of around £10k a year. Even big wins on lotteries etc seem to have only a short term uplifting effect before individuals revert to whatever their happiness level used to be before hand. Money it seems does not buy happiness. However, rich people are in general happier than poor ones and so the famous quote from Sophie Tucker is also true:

“I’ve been rich, and I’ve been poor. Rich is better.”

80% of the variation in happiness can be linked to six factors

According to Helliwell (2003) the majority of variability in happiness is associated with:

divorce rate

unemployment rate

level of trust

membership of non-religious organisations

quality of government fraction

believing in God

How happy are we and what and who can make us most happy?

Believe it or not there is a extensive World database of the happiness levels and trends shown in different countries between 1946 and now. It is maintained by Dutch scientists at Erasmus University (R. Veenhoven –http://worlddatabaseofhappiness.eur.nl). In general this shows that the rich countries in the developed world are happier than the poor ones in the third world. Interestingly though, average happiness trends between 1973 and 2004 show that Italy and Denmark have had the largest increases in this period with USA, Luxembourg and France improving slightly less. The UK and Ireland, Holland and Germany were static and Japan and Belgium had a decline.

Richard Layard in his book lists the impact that different activities can have on our happiness. Surprise, surprise, sex comes out on top although of course the amount of time spent having it per day is relatively small. In terms of the different people who boost out happiness, friends come out better than partners and bosses come last!

Indeed, as would be predicted from the strong genetic influence on happiness, individuals tend to be relatively stable in terms of the general patterns and levels experienced during life. What works out best is where individuals fluctuate relatively little in terms of their moods as opposed to those who can vacillate wildly between extreme happiness and extreme depression. Artistic individuals in particular tend to fall into this latter category although research suggests that such fluctuations may not be essential for inspiring their creativity.

However, this is not to say that there are not some general societal and economic factors that boost happiness reliably. These include societies where individuals have a high degree of trust in one another and their governments and where there is a degree of egalitarianism in terms of individual earnings (i.e. not a massive rich/poor divide). People also benefit from even very small unexpected bonuses such as finding money on the street or other places. A classic experiment showed that people who unexpectedly found a 10c coin in a photocopier when they used it, as opposed to those who did not, reported at interview a greater level of contentment with their whole life for the last 20-30 years! Recent events and expectations can indeed colour the way you view your whole life on an almost day to day basis. Self-reported relative happiness can be extremely fickle!

And yes, the popular view that happiness and intelligence are negatively correlated has received some experimental support with people performing tasks better when they adopt a relatively sceptical negative viewpoint than when they are very happy. Rather like the intense phase of love therefore, intense positive emotions can be detrimental to both judgements and problem solving. However, in the long run people with higher average happiness tend to be more successful in all aspects of their lives and they also live longer, possibly because a happy demeanour tends to boost immunocompetance.

Judging happiness

We appear to be very bad at predicting whether major life events which we expect to make us happy will actually do so. The reason for this is not well understood although some consider it simply to be because while a single event like the purchase or a house or a car or taking a holiday might be pleasant the rest of our life stays the same and that can be enough to quickly outweigh the new pleasant experience. Daniel Nettles has come up with another somewhat radical idea that we have evolved to get happiness predictions wrong more often than not so that we are maximally competitive to help our survival. If we were too good at planning happiness outcomes perhaps we might just end up being too laid back to get on in life. Interesting thought!

Happy pheromones?

What we are good at doing is detecting whether other people are happy, not just by their smile but also by their smell. It seems being happy or unhappy alters our biochemistry and therefore our smell. In some animals it has now been established that they produce glandular secretions signalling both “alarm” and “contentment”. Perhaps we do the same. I recent met Patrick Pageat at a conference in Asahikawa in Japan and he has formed a research company in France (Phérosynthèse) that is isolating “appeasement” pheromones to help control stress and anxiety in companion and domestic animals (Feliway for cats, Dog appeasement pheromone – DAP – for dogs and equine appeasement pheromone – EAP – for horses. He is currently working on one he claims is secreted from the breast of nursing women and that reduces anxiety in us – I assume this may be called HAPPY)!

But leaving happy smells aside for a moment I will now move on to the second part of my lecture concerning whether biomedical advances are going to make us happier in the near future.

Can biomedical science live up to our expectations of good mental well-being?

Both media and biomedical scientists say “magic bullets” are just around the corner but are they? Are we better off reducing our expectations and relying more on lifestyle changes? Can we really expect a “drug

me happy” scenario or are we mainly going to have to do it the hard way and rely on self-help and lifestyle changes?

Is it realistic to expect “magic-bullet drugs” to improve our Love lives, be happy when we want to, be able to eat, drink and be merry without suffering the consequences, be free of stress, anxiety and depression, have a fantastic memory and not suffer from age or neurodegenerative conditions that rob us of key mental faculties? Is there going to be a pill that allows us to be happy 24/7?

What should I hope have become obvious from my lectures is that we still have much to learn about how the brain works normally, let alone what can cause it to malfunction and lead to mental disorders. So even with perhaps 50,000 Neuroscientists out there trying to crack their own particular version of the brain’s Enigma code it is perhaps fitting to consider what science has already done to influence our happiness and what more it might achieve in the near future and what it probably will not. Along side of this we need to balance this “reliance on science” dogma with what can loosely be termed a more self-centred policy of “self-help”.

While it may have often appeared as if it has been science that controls man’s destiny it merely provides understanding and some degree of control over the physical world. It is after all only a tool, just like a spade or a knife, designed to help us live our lives and perhaps also revel in achieving some degree of understanding about the wonders of our universe and even of ourselves.

Sex and love

Designer aphrodisiacs are big business and while Viagra, Cialis and Levitra are ostensibly for males with erectile dysfunction they are widely used in a recreational sense. However, these drugs target performance rather than desire and work mainly in males. Now there is an entirely new kid on the block that looks set to revolutionise the sex enhancer market for both men and women. It is called PT-141 and is in the final phase of clinical trials

PT-141 is a derivative of Melanotan II that is called the “Barbie drug” originally developed by Palatin in the USA. This drug not only boosts desire but makes you lose weight, protects you from the sun and a whole load of other things. However, the company created a derivative of this which only influences sexual desire and performance. From an article in New York magazine in 2005 these are the kinds of comments people involved in human trials made:

“With PT-141, you feel good, not only sexually aroused,”

“you feel younger and more energetic.”

“It helped the libido. So you have the urge and the desire.... You get this humming feeling; you’re ready to take your pants off and go.”

“Tales of pharmaceutically induced sexual prowess among 58-year-olds are common enough in the age of the Little Blue Pill, but they don’t typically involve quite so urgent a repertoire of humming, throbbing, tingling, and double-dipping. Or as patient 128 put it: “My wife knows. She can tell the difference between Viagra and PT-141.”

The drug works very well in women too and one of my colleagues, Jim Pfaus, in Canada did the original work on female rats showing that PT-141 greatly enhanced the extent to which female rats invited sex from males and would even take the initiative themselves on occasion.

However, sex is one thing, finding love is quite another! There are no pills under development for making

people fall in love and as most of us know full well, science is a long way from predicting love matches let alone controlling them.

In my lecture “Addicted to love, beauty or sex?” (14th February 2005) I discussed data suggesting that the so called “make me happy drug” PROZAC may actually suppress our ability to fall in love since it boosts serotonin levels in the brain. Research has shown that falling in love lowers levels of this transmitter to make us more impulsive.

Eat, drink, smoke, gamble and be merry

There are many claims of a “magic bullet” anti-obesity drug being just around the corner. However in my lecture “Diet and obesity: the food of destruction or manna from the Gods” (11th November, 2004) I showed that the radical slimming potion portrayed in the film “The Nutty Professor” starring Eddie Murphy is a Hollywood fiction.

The best that any drug developed so far can do is to promote a 5% weight loss before compensatory mechanisms kick in. This will reduce health risks from cardiovascular disease and type 2 diabetes but will not make a fat person thin. The only medical intervention that can achieve the latter is bariatric surgery and that is both life threatening and not that pleasant to live with either. Realistically, millions of years of evolution have designed all animals, including humans, to feast when food is freely available because for most species there is a good deal of uncertainty as to when the next meal is going to come along. Obviously for humans in the developed world that meal can be made available for a small cost any time of the day or night. There are multiple control mechanisms in the gut and brain that allow this feasting behaviour and so ultimately the only drug that could challenge surgery for effectiveness would have to target many of them simultaneously. This could cause significant side effects.

So while increased ill health and reduced self-esteem, life expectancy and happiness are all associated with the growing tide of obesity which now affects up to one-third of the population in some countries, biomedical science is far from providing a simple pharmaceutical remedy.

Obesity in the vast majority of cases is simply the result of taking too little exercise and eating too many high caloric foods. Interestingly, while it is true that eating food is a highly pleasurable experience which activates the brain dopaminergic reward systems so does exercise. However the time factor for putting on calories through eating is far shorter than burning them off through exercise!

So here is a very clear example where lifestyle changes rather than drugs are likely to be the most effect remedy in controlling the obesity problem for some time to come.

With alcohol and smoking addictions there are also no easy quick drug fixes, although new drug developments such as Rimonabant are claimed to suppress all addictive urges by acting to reduce activity in brain reward systems. One has to question though whether promoting anhedonia is exactly improving “quality of life”.

Finally gambling and general risk taking is also something where drug therapies have so far had only limited success, again by acting to generally suppress the pleasure we get out of any activity (see my lecture “Why do we gamble and take needless risks” March 2006).

Mental health and freedom from stress, anxiety and depression

One of the most impressive success stories in human medical advances has been our ability to treat the

mentally ill. There are far fewer people in mental institutions now than at any time. The discovery of chlorpromazine for treatment of schizophrenia, lithium and tricyclic compounds for depression and diazepam for anxiety have all allowed many individuals to lead a normal life whereas in the past they would have probably been confined in a mental Institution.

However, further advances are still only coming on relatively slowly. 1 in 5 of us will suffer from a clinical anxiety or depressive disorder during our lives and in any week 1 in 10 of us are seriously depressed. Further more, as I have outlined in previous lectures, the nature of the society in which we live has meant that problems are on the increase ("Stress, anxiety and depression" – 7th October 2004 ; and "When I was a child I thought as a child, I acted as a child….." – 6th April 2006).

PROZAC and other serotonin selective uptake inhibitors (SSRIs) are often effective but take time to work. The reason they take so long to work seems to be that it is not simply their ability to raise serotonin levels in the brain to allow better control over impulses and emotions. Rather, they appear to promote growth of new connections within brain areas such as the frontal cortex which ultimately put us back in control. This is why the treatment takes so long to work.

28 million people in the USA take antidepressants and in the UK so many of us take PROZAC that it is detectable in drinking water. These drugs are not without their side effects, particularly in terms of the sex drive and perhaps even making it difficult to fall in love.

Brain stimulation of happiness centres is now also being used to help treat individuals who fail to respond to drugs. This uses a method called transcranial magnetic stimulation and can allow the localised activation of the left prefrontal cortex to promote improved feelings of contentment.

In terms of the potential future directions for biomedical research in this area it seems that new approaches for the treatment of anxiety and depression disorders will focus more on targeted promotion of re-growth of connections in brain emotion control systems. However, any new generation of drugs will only help you cope they do not solve the problem.

It is possible that gene therapy approaches will be developed to lessen our predisposition towards stressful life events triggering depression. For example different variants of the serotonin transporter gene (short vs long) which helps regulate the amount of serotonin in the brain could be utilised. However, gene therapy still has considerable risks and different forms of this particular gene do not cause depression they only make it more likely that if you have a stressful life history you will develop a depressive or anxiety disorder.

So even with the most sophisticated drug or gene therapies we may be able to develop you need to identify the problems which you are having difficulty coping with and avoid them. Animal research shows very clearly that positive action is better than passive coping or simple avoidance. When animals just "roll over and take it" rather than adopt and active interaction strategy they are more likely to die from the effects of chronic stress!

Our parents, education systems and work environments all need to help us learn to see the glass half-full rather than half-empty and to take positive steps towards dealing with stress. We also need to use social buffering more. Both animal and human experiments show that your stress/anxiety levels are reduced just by being with another individual who is calm, but not with one who is also anxious. The benefits of exercise, relaxation techniques and a healthy diet are also well established.

Lastly, developing a sense of purpose is also highly beneficial. This is normally viewed in terms of having a

strong religious belief and this does indeed seem to help. But it can also be viewed in the context of membership of non-religious organisations with laudable aims. Of course many individuals are self-motivated simply by their own personal desire for some form of lasting achievement. However, the latter is often easily blown off the rails.

Become a mastermind

In my lecture “Memories are made of this but what about intellect?” (4th December, 2003) I concluded that are no where near to developing effective cognitive enhancer drugs. The main reason for this is that we simply do not understand sufficient detail of how the brain learns, remembers and integrates information. There are however significant efforts to discover drugs that improve our cognitive faculties although, like Viagra, the justification for this research is to treat people with problems due to brain damage or age or neurodegenerative disease induced cognitive decline. Just as with Viagra though it is easy to see how such a drug, if successful and with minimal side effects, could end up being widely used for work or even leisure purposes.

As we begin to understand the importance of rhythmic and temporal correlation changes in the brain it seems possible that either drugs or self-learning (biofeedback) might help us to improve cognitive function through helping to control and regulate these holistic processing systems within the brain. But we still have along way to go in this respect.

In the meantime we will have to continue to learn and use information the hard way through a lengthy period of education. So hopefully attendance at Gresham lectures will continue to increase!

Never get old or lose your mind

Will drugs ever allow us to live to 200? I dealt with the problem of ageing in my lecture entitled: “Turning back the hands of time: ageing gracefully” (23rd March, 2004). We are certainly living longer and it is thought the human body is capable of surviving well into the 100s if we treat it the right way. Our cells can only divide a number of times during life and then senescence sets in. This division process is controlled by tail-like nucleotide protein structures at the ends of the chromosomes called telomeres. These are numerous TTAGGG tandem repeats which get knocked off one by one as cells divide again and again. To some extent you can tell how long someone has got to live from the length of their telomeres. Telomeres can be protected by enzyme telomerases and so attempts may be made to develop drugs which boost telomerase activity so that cells keep on dividing and ageing is slowed. So called immortal species such as sharks produce high levels of telomerase. However, this is also what cancer cells do (they have high telomerase levels) and so it will be tricky avoid cancers developing using this approach!

Cardiovascular problems are obviously a major cause of death and while treatments have improved considerably in recent years this is still a significant rate-limiting factor to achieving greater life span. From my previous lectures you will remember that people tend to live longer if they possess gene variants that help protect against the damaging effects of low density lipoprotein cholesterol. One of these genes is ApoE2 and another is cholesterol ester transfer protein (CETP). However, even were we capable of giving these protective variants to individuals who don’t have them it is still estimated that average life span would only increase by around 15 years and even if we cured all human diseases, not just cardiovascular ones!

Growth and repair factor promoting drugs are also a major target for anti-ageing therapies to help both with body and brain. In general, growth factor activity declines during ageing and this affects growth and development of cells throughout the body and means our bodies are also less able to repair themselves following injury or simple wear and tear. There is currently a major focus on taking human growth hormone at extortionate costs. Levels of this hormone decline during ageing and some studies have indicated organ, muscle and skin rejuvenation and prolonged life as a result of taking supplements. Animal studies though have revealed that lack of growth hormone developmentally (causing dwarfism etc) can actually prolong

life. There may even be increased cancer risks associated with taking growth factor enhancing drugs. So the large numbers of rich people in the USA injecting themselves with growth hormone at costs in excess of $100,000 a year many not necessarily be doing themselves much good in the long run, although there do certainly seem to be short-term vitality gains.

Since only 25% of ageing process is down to your genes per se the search for gene candidates to enhance longevity, other than helping to reduce disease problems, is not likely to be of great importance

Instead, it is still clearly lifestyle factors that hold the most pragmatic key to living longer, if you want to that is. So if you do want to live longer and/or in better health you need to avoid or limit smoking, drinking, drugs and high stress. You also need to eat a proper balanced diet and limit your calorie intake. Animal studies actually show that controlled caloric restriction can almost double life span although it has not been proven to do so yet in humans. Eating far too little can shorten your life though and arguably removing enjoyment of food from the agenda is also taking away an important source of pleasure and happiness.

Eating foods or taking pills rich in anti-oxidants such as vitamins C and E have been suggested to help protect our bodies from the ravages of ageing, as have moderate amounts of chocolate and red wine which contain anti-oxidant phenols – and might also give you pleasure as well!

Avoiding chronic stress is very important since it not only compromises your immune system and can damage your body but can also lead to depression and anxiety disorders which can shorten your life.

As far as trying to avoid problems with brain senescence then the “use it or lose it” maxim is by far the most effective lifestyle advice. It seems that people who use their brains a lot alter the way they process information as they get older so that they utilise more of it. This may help protect them from having problems with age-associated cognitive decline. Those individuals who do not exercise their mental faculties so much retain their more restricted youthful way of processing information but the ageing brain is not able to function so effectively this way and cognitive decline can therefore occur.

A final reminder piece of advice for those of you who want to live longer is “Be happy!”. Happy people tend to live longer than unhappy ones!

Neurodegenerative disorders

While there has been good success with at least controlling Parkinson’s disease in the majority of individuals this reflects the fact that it has a highly specific pattern of degeneration affecting one particular neurotransmitter system, dopamine. However current drugs do not seem to be so effective for long-term treatment and putative therapies for reversing or preventing the damage, as opposed to replacing the depleted transmitter, are still a long way off

Alzheimer’s still remains top target for biomedical research and while more is understood about genetic contributions to this the development of effective treatments is still a long way off. With this debilitating disease, as well as other neurodegenerative disorders, the main emphasis must be to understand its cause and to prevent it occurring. Once the damage has been done the logistics of effective repair are quite daunting.

As with all cases of brain damage, because the brain maintains flexibility throughout life to form new connections, the simple adage of keeping the brain working and active to try and overcome problems is just as an important one in the context of neurodegenerative diseases as it is for normal ageing.

Soma – the full time happiness drug?

There are I am sure very few of you in the audience who have not while at school or University been required to read Aldous Huxley's "Brave New World". But just to remind everyone of one of the major stabilisers of the New World society was a happiness drug called "soma". This promoted a permanent feel good factor that effectively made all citizens both happy and unquestioning of the way their lives were controlled. Some might argue a "brain dead" option and shudder – as indeed the central character of the story John "Savage" did. The controller of the society admits that happiness has been achieved by promoting comfort at the expense of truth and beauty. Art and science are impossible because they often involve challenging experiences which are not necessarily happy. John (the Savage) eventually exclaims:

"But I don't want comfort. I want God, I want poetry, I want real danger, I want freedom, I want goodness, I want sin."

"In fact," said Mustapha Mond (the controller), "your'e claiming the right to be unhappy."

"All right then," said the savage defiantly, "I'm claiming the right to be unhappy."

Continues the controller: "Not to mention the right to grow old and ugly and impotent, the right to have syphilis and cancer, the right to have too little to eat, the right to be lousy, the right to live in constant apprehension of what may happen tomorrow, the right to catch typhoid, the right to be tortured by unspeakable pains of every kind."

There was a long silence. "I claim them all," said the savage at last.

Of course we have PROZAC to help us deal with depression and anxiety, cocaine, LSD, heroin, ecstasy and many others to help stimulate various components of our brain's pleasure system to make us feel euphoric or lose touch with unacceptable reality. But no one would argue that they promote happiness, more an escape from negative feelings.

Yes, you can have transcranial magnetic stimulation (TMS) of your left prefrontal cortex and this, as I have already mentioned, makes you feel happy and is beginning to be used in the treatment of depression. However, this is hardly and routine procedure although with the number of wires you see coming out of people's heads these days with MP3 players etc I suppose having a TMS box in one pocket connected to your forehead and an MP3 or mobile phone in the other connected to your ears might be deemed acceptable. Perhaps they might even get linked up into a single device so all music and all phone calls make you feel happy!

Work on appeasement pheromones may even result in us sniffing happiness from a bottle!

The simple fact though is that unless happiness is self-generated it is not sustainable and therefore drugs and other interventions in the working of the human brain can at best only make it more likely that life experiences will be viewed in a positive rather than a negative way. Indeed, some would argue also that experience of happiness is only possible if you are capable of experiencing unhappiness or sadness as well.

So "drug me happy" is not on the biomedical agenda and in the end developing and maintaining a happy demeanour will require positive self help and where that fails seeking help from psychotherapists and psychiatrists who practice positive psychology approaches.

Of course it just needs England to win the world cup to result in boundless national euphoria in this country for several months without the assistance of drugs (other than perhaps alcohol). However, the problem is the majority of nations have to lose in such competitions and they will experience more negative feelings instead. Perhaps someone needs to find a game where everyone wins but does not expect to. Quite a challenge, but probably far easier than finding an effective “soma” drug!

Some conclusions:

- Happiness is largely genetic
- It has different levels
- Happy people smell different and have a more active left frontal cortex
- We are not good at predicting successful happiness outcomes
- Trust, good relationships, job and financial security and religious belief help
- Sex is still the number one happiness booster…and there are more pills to help
- ….but not to find love!
- Money does not buy happiness…but rich is still better!
- Happiness is strongly influenced by expectations
- Drug me happy is not a realistic future option
- Lifestyle factors will always play a major role
- We should put more resources into promotion of self-help
- We should expect less of medical science and our football teams
- ….and more of ourselves

Selected References

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