

THE INVESTOR

Brain

R&D MARK WESTFIELD

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An Australian start-up is creating a database of the brain's workings that may help revolutionise the global drug industry.

EVIAN GORDON WAS STUDYING medicine and science and was on course to be a heart specialist when he saw a fossilised skull that had been unearthed at Taung, in southern Africa, in 1924 and later identified by Australian anatomist Raymond Dart as the "missing link" between ape and man. Gordon was amazed by the skull from a 5 million-year-old hominid called *australopithecus*, who walked upright and used his hands with great dexterity compared with earlier evolutionary stages.

"The size and structure of the skull showed that the brain of this person had undergone a huge reorganisation from its predecessor," Gordon recalls, 28 years after what was to be a life-changing experience. "I had been studying serum lipids and intended to be a heart specialist but after seeing that fossil, I immediately decided to switch to neuroscience to study the brain."

Much has happened in the meantime to Gordon and to the lives of hundreds of people with brain disorders in Australia and overseas whom he has been able to help as a result of his decision back in 1976.

Emilie Jay, 33, is one. She was leaving a phone box to walk back to her home late at night in Sydney's Rooty Hill two years ago when she was attacked from behind and struck hard on the side of her head. She fell unconscious to the ground and later needed reconstructive surgery to repair broken bones

around her right eye. The more serious damage was inside her head.

Three months later, after being urged by friends to get help because she couldn't concentrate and often burst into tears during conversations, she saw medical psychologist Dr Kim Felmingham at Sydney's Westmead Hospital. Felmingham diagnosed Jay with post-traumatic stress disorder, a condition becoming increasingly common in Australia but particularly in the United States after September 11, 2001. In order to be sure of her assessment and to confirm Jay wasn't suffering from brain damage, Felmingham referred her to a group called the Brain Resource Company, run by Dr Evian Gordon - by now in an advanced state of evolution from cardiologist to neuroscientist and entrepreneur.

After his experience with the fossil, Gordon changed courses, graduated with four science degrees and a medical degree from Johannesburg's University of Witwatersrand and emigrated to Australia in 1982 to take the position of founding director of Westmead Hospital's Brain Dynamics Centre.

The hospital was only three or four years old and a hotbed of ideas and research. "It had none of the territorial attitudes of more established institutions," Gordon says. "It was full of young, dynamic radiologists, psychiatrists, psychologists and physicists and we were able to come together to brainstorm ways to try to solve problems of the body's most complex organ.

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EVIAN GORDON ON HIS FIRST YEARS AT SYDNEY'S WESTMEAD HOSPITAL



"What I needed to help bring them together, because of their different disciplines, was to build a database that each could analyse in their own way and compare how brain-disorder patients reacted to certain drugs, and to get a better idea of how the whole brain worked as a system - not just parts of it."

Although he didn't know it at the time, this was the beginning of what became a quest to build the world's first and most comprehensive database on the human brain to use as a powerful tool to better understand and treat disorders.

At both Westmead Hospital and the BRC's busy offices in inner-city Ultimo, Emilie Jay did a series of tests to help Felmingham determine whether her diagnosis was correct. "As a result of the Brain Resource Co's standardised tests analysis of Emilie's results, compared with matched examples in the database, we were able to rule out organic damage and target our treatment to reduce Emilie's anxiety. It gave us a much clearer insight into her condition," says Felmingham. "You can never exclude brain damage in cases like this, but we felt there was a very good chance with Emilie that this wasn't the case."

Gordon and his team had subjected Jay to a number of tests, including an electro-



GREY MATTER

Emilie Jay was diagnosed with post-traumatic stress disorder after being attacked outside this Sydney phone booth. There were also concerns she had suffered brain damage, so she was referred to Evian Gordon. He and his team subjected Jay to a series of tests and concluded that her anxiety was not the result of brain damage but due to a disturbance to the fear networks in her brain's subcortex.



encephalograph, or EEG, measurements of the body's anxiety (sweat rate), tests of memory, attention and planning, and fed the results into the database. They were able to conclude that Jay's anxiety was due to a disturbance to her fear networks in her brain's subcortex, the central part that processes emotions. This part of the brain is far harder to read and requires analysis of information from a functional magnetic resonance imaging (fMRI) machine to see what parts "light up" in response to tests, such as viewing pictures or images.

The cortex, or the top of the brain, processes signals from the eyes and ears

for visual and auditory perception and can more easily be read via EEG, which is conducted by using a cap fitted with a number of recording discs placed on the scalp to monitor electrical rhythms.

Although EEGs have been used in various forms to read electrical signals in the cortex for 125 years, determining what was actually happening has been "tenuous", according to Gordon.

This form of testing is soon to become more precise and reliable after a group of scientists attached to the BRC, led by Professor Peter Robinson of the School of Physics at the University of Sydney, won the 2003 interdisciplinary Eureka Prize for developing a computer model of the brain. It is expected to take the reading of electrical activity in the brain to new levels. The rest of the team comprised a psychiatrist, Professor Jim Wright, a mathematician and physicist, Dr Chris Rennie, and Gordon.

The head of the post-traumatic stress disorder unit at Westmead, Professor Richard Bryant, says Gordon's BRC is not just "on the right track, but creating the track".

"PTSD is not a homogeneous disorder, there are a number of subtypes. To identify the type correctly and treat it, you need a very

large number of cases. This database allows comparative research that otherwise would have been impossible."

Jay told *The Bulletin*: "Before I had the treatment, in a range of one to 10, I probably felt about 6. Now I'm 8 to 8.5. I feel a lot better. It has markedly reduced my anxiety."

The brain is the last frontier of the body and still holds its mysteries. It is highly complex and has more processing power than the world's most powerful computer. Yet, it can be disrupted easily and leave its owner anything from helpless to forgetful, anxious, suicidal, highly stressed or combinations of all.

Dementia, depression, Alzheimer's disease, post-traumatic stress disorder, schizophrenia, attention deficit disorder, brain injuries and childhood stress are afflictions that the medical profession has yet to come to fully understand and treat with certainty. Gordon is using his BRC database to help reduce costly and time-consuming trial and error procedures in treating them.

The power of Gordon's database lies in its size, with information on more than 3000 cases, and that it is standardised. It relies on a sharing of information provided by laboratories in Australia, The Netherlands, Britain

and the US. Each laboratory collects identical information using the same equipment, tests and task instructions. As Gordon's database grows with more cases and more participating labs, the more accurate it becomes. The key was for Gordon, over the years, to win agreement among a group of eminent scientists from a number of disciplines on exactly what information to collect.

All patients referred to the BRC, whether suffering from dementia or schizophrenia, or healthy specimens included for comparison purposes, undergo the same tests. The subjects are referred to only by ID codes.

The information stored in IBM servers at Ultimo includes personal and medical histories, personality traits, readouts of electrical brain

interviewing 200 brain scientists around the world. He called it *Models of the Human Brain* and it was shown on SBS in 1996.

"What struck me was how super specialised it all was. No one was putting the pieces together." Gordon calls this tendency among brain specialists "neural epicentrism", a tendency by scientists to regard their discipline as the epicentre.

"Without some effort to pull all the pieces together you can't conceive how the whole brain works as a dynamic system." The experience convinced him that a global standardised database that brought the pieces together was the logical next step. He and his colleagues at Westmead had been using a localised information bank for the

Ex-Wallaby and Citigroup banker Simon Poidevin arranged a further \$4m through a placement to some institutions. Another link Poidevin provided was to Professor Tony Sinskey at the Massachusetts Institute of Technology, a leading player in medical research. Sinskey has recently joined the company's scientific advisory committee, chaired by Professor Arthur Toga from the University of California, Los Angeles. Its main board includes former prime minister Paul Keating.

With the money from the 2001 float, Gordon set about consulting with a group of 40 scientists to determine the concepts and details that would shape the international database, including standardised tests. The key experts were Professor Ed Bullmore from Cambridge University, Professor Ruben Gur from the University of Pennsylvania, Professor Elkhonon Goldberg from New York University, Professor Peter Schofield, director of the Prince of Wales Neuroscience Institute in Sydney, and Associate Professor Richard Clark from Flinders University, Adelaide.

Another factor that has driven this style of evidence-based analysis of illnesses has been the tendency in the US at least to start focusing research on personalised medicine. In two recent papers, the Food and Drug Administration has urged the pharmaceutical companies to adopt a personalised treatment model to make their drugs more targeted to individual responses, rather than the trial-and-error style.

Spending on drug research is running at \$33bn a year and growing at a compound rate of 10% a year. This means drugs cost on average \$870m to develop and bring to market, with the pharmaceutical companies looking to maximise returns. In doing so, they miss the mark for a sizeable proportion of patients they aim to treat. Recent studies have shown that popular drugs such as antidepressants work for between 50% and 80% of patients, and interferons for 30% to 70%.

Ironically, too, the FDA reports that fewer drugs are coming before the agency for approval. The director of the FDA's centre for drug evaluation and research, Janet Woodcock, has said that "using genomic [DNA, or genetic] testing to guide therapy will constitute a significant shift towards finetuning individual therapy".

Dr Caroline Kovac, general manager of healthcare and life sciences at computer maker IBM, which is investing heavily to develop solutions for the healthcare industry, reckons the pharmaceutical industry is "in crisis" over the so-called blockbuster drugs. "The blockbuster won't go away, but the model will change and those companies that don't get it may not be around."

Evian Gordon hopes his more modest contribution to health analysis and treatment will complement the trend Woodcock and Kovac have identified. "We're either seriously right, or also-rans," he says. ●



CEREBRAL THINKER

Evian Gordon is both neuroscientist and entrepreneur

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EVIAN GORDON BRAIN RESOURCE COMPANY

function, brain structure and blood flow during the tests, cognition, and genetics of patients provided by the 11 participating laboratories. By comparing the results of tests done by new patients, such as Jay, with the other 3000 case histories, the database can be used to assess the disorder and how to treat it with considerable accuracy.

The ultimate objective, Gordon says, is not only to accurately determine the disorder the patient is suffering from, but also the appropriate medication. In cases of childhood attention deficit disorder, for instance, Gordon says that preliminary results from BRC's database can predict this with 92% accuracy. Similar studies are under way for depression and Alzheimer's disease.

During his time at Westmead's Brain Dynamics Centre, Gordon moved another stage in his personal evolution in 1995 when he was invited by the Professional and Graduate Education consortium of 11 Australian universities to put together a 14-part television series on the brain,

previous 15 years, but he believed brain disorders could only be tackled adequately if as much information and intellectual input as possible from around the world was used. "The [TV] series was the final catalyst which put me on course to set up a database on an international scale."

The next challenge was to find the money. He was offered funding by an Australian venture capital group, but on the advice of a telecommunications analyst with Citigroup, Dan Segal, opted instead to raise funds through a float to leave open the potential to raise further money in the future from a shareholder base. Segal left the bank and joined Gordon as commercial director at BRC just before the August 2001 float. The company raised \$5m to finance development of the database. Gordon and Segal were among the founding investors in the company, along with Queensland Investment Corporation, Westmead Hospital, the University of Sydney, the Institute of Psychiatry in London and 20 scientists globally.