



EDITORIAL

Michael Morgan

Euro-Ataxia 17 features just a little science and a lot of personal reflection. Rest assured, the scientists will have their say at the forthcoming EURO-ATAXIA AGM in Westende, Belgium, at the end of October. For now though, let's let the inmates take over the asylum...

Last March I attended the 42nd AGM of the National Ataxia Foundation in Orange County, California. The conference itself followed more or less the same format as our own in Europe – medical/scientific reports first in the morning, followed by talks on 'living with ataxia' in the afternoon. And of course the ataxic people in the US are very friendly – well worth the visit even though I for one found the air journey all the way to LA and back quite dreadful. See inside for a full report. Incidentally next year's conference is being held not just so far away – in Biloxi, Mississippi. Maybe we should try to arrange a contingent from Europe to go over for it? If so we should start planning soon, so I add some more details from the NAF Website (<http://www.ataxia.org>). If anyone's interested let me know. And from the American AGM we reprint Dr. Massimo Pandolfo's report on *Friedreich's Ataxia: New Developments and Perspectives*, which gives a good summary of the current state of play.

Some ataxic people find faith and a belief in God at home or abroad. Monika Müller tells inside of her journeys to Sathya Sai Baba in Southern India, and what this means to her.

Anybody with ataxia who has ever used a computer will tell you that poor dexterity and dysarthria combine to make a major problem in getting text on screen. Poor dexterity means poor keyboard skills. Dysarthria and slurred speech makes the obvious alternative – voice recognition software – a daunting prospect to master. Peter Bayliss writes inside of his experiences with DragonDictate, one of the most popular and efficient programs available.

Finally, the 11th Annual General Meeting of EURO-ATAXIA will be held in Westende, Belgium, between 29th – 31st October, 1999. Full details inside.

DRUG TRIALS FOR FRIEDREICH'S ATAXIA

Michel Koenig, IGBMC, Strasbourg, France

Following the identification of the gene responsible for Friedreich's ataxia, the mechanism causing the heart defect has been in part elucidated. In all likelihood, the defect results from mitochondrial dysfunction caused by free radicals produced by an abnormal metabolism of mitochondrial iron and iron-sulphur proteins. These proteins and iron are necessary for electron transport within the mitochondria, the driving force for energy production in living cells. Out-routed electrons interact with a large variety of molecules, including oxygen, to form free radicals,

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which are harmful to the cell through a process called oxidative stress. This experimental observation made in the laboratory has led to the proposal of specific anti-oxidant administration as treatment for Friedreich's ataxia. Alternatively, iron clearing molecules (called iron-chelators) have been proposed as well. Accordingly, several therapeutic trials have been initiated during the last 6 months. Some details of their implementation have been reported at the annual meeting of the French Friedreich's Ataxia Association (AFAF, April 11th in Beaune, close to Lyon) and at the Friedreich's ataxia international meeting, held in Bethesda (close to Washington, April 30th-May 2nd) and sponsored by FARA (Friedreich's ataxia research association) and the NIH (US national institute of health). The French trial has been discussed at length at the AFAF meeting. The trial has been submitted at the Direction de la Recherche Clinique de l'Assistance Publique de Paris, by the groups of Arnold Munnich (Hôpital Necker-Enfants Malades) and Alexis Brice (Hôpital de la Salpêtrière) and was accepted. For administrative reasons (sic), implementation of this trial had been slow. It is an open trial (all patients in the trial are treated with the same drug at the same dose) and it includes 50 adults and 30 children. The trial started on April 26th and seven patients are included every week, indicating that inclusion must have finished by late June. Inclusion means that patients are clinically evaluated by the same methods that will be used for evaluation of the drug efficacy, followed by initiation of the treatment. The trial will last one year. Evaluation will be performed at 3, 6 and 9 months and at the end of the trial. Due to the evaluation constraints, only patients that were still able to walk were selected. The evaluation includes, among other things, a thorough clinical evaluation, muscle tone measurements, eye movement measurements and echocardiography. Statistical analysis of the data will be done at six months and at the end of the trial. The drug, Idebenone (5mg/kg/day), is an anti-oxidant derived from ubiquinone (or Coenzyme Q10). Idebenone is a Coenzyme Q with a short side chain (CoQ4) and therefore crosses better membranes than CoQ10. In particular, Idebenone is expected to cross the 'blood-brain barrier' (in this case 'brain' also includes the spinal cord). The commercial name of the drug is Mnesis and is produced by Takara Laboratories (Japan). The only country where this drug has received Market Approval (but for another disease, Alzheimer disease) is Italy, causing some difficulties in getting it. Two points relative to this trial have been stressed during the AFAF meeting. First, there is currently no definitive proof that Idebenone is indeed effective in Friedreich's ataxia. The current trial is therefore made to answer this question. Any problem during the trial may preclude for long our possibilities to answer this crucial question. Second, all patients included in the trial have accepted not to take any other drug during the trial (other anti-oxidants, iron chelators or others), in

order to avoid interference with the drug efficacy evaluation. This point is very important since drugs acting in the same pathway may have competitive effect which may obscure any beneficial effect of Idebenone. The take home message for the patients not enrolled in the trial was to wait for six months when the first data will be statistically evaluated. In case of positive results, the generalisation of the treatment should enter within the frame of a larger, multicentric evaluation trial, in order to collect further data on Idebenone efficacy, such as long term efficacy, interindividual variations, expansion length dependence, etc... Having said this, preliminary results on 5 Friedreich's ataxia children with progressive cardiomyopathy and treated before the trial are encouraging, suggesting a stabilisation or even a regression of the cardiomyopathy (Rustin et al. Lancet, in press). Any conclusion on the neurological symptoms would be premature at present. However, clinicians keep the right to decide to initiate an Idebenone treatment in individual cases warranted by the progression of the heart disease.

Another trial using anti-oxidants has been initiated by the group of Anthony Shapira, London. The drugs are a combination of Coenzyme Q10 (400mg/day) and vitamin E (2000 IU/day). The originality of the trial is the use of 31 phosphorus magnetic resonance spectroscopy which is a direct mean to measure mitochondrial energy production in heart and muscle, and which, according to the saying of Anthony Shapira, detects anomalies in the muscles of untreated Friedreich's ataxia patients. Here again, the trial is scheduled for one year.

One trial using iron chelators has been initiated in Salt Lake City, by the group of Julie Smith and Jerry Kaplan. This is a one year, double blind trial, indicating that half of the patients will receive a placebo and the other half will receive the drug, in this case Desferal (desferrioxamine). Desferal is a daily injected drug. Pre and post treatment investigations include a heart endomyocardial biopsy, for direct evaluation of the evolution of the heart pathology and iron deposits, and haematological monitoring in order to evaluate possible side effects of iron deprivation. Seven patients were enrolled in this trial, as of April 30.

Needless to say, results from the coming year will be scrutinised and urgently debated.

NAF ANNUAL MEMBERSHIP MEETING 1999

Michael Morgan

With a total membership of 3200 the National Ataxia Foundation in the US is widely held to be the best-supported and best-organised ataxia group of them all. Last March I attended their 42nd AGM in Orange County, California. What struck me first of all was the scale of the operation. Having organised a EURO-ATAXIA conference myself, of say, 35-45 people in

2000 ANNUAL MEMBERSHIP MEETING OF THE NATIONAL ATAXIA FOUNDATION

The Mississippi Chapter would like to invite you to the 'Playground of the South' on the weekend of March 24-26, 2000. The location will be the Imperial Palace Hotel & Casino in Biloxi, Mississippi.

The Imperial has 1,100 sleeping rooms, 50 of which are accessible. There are 18 specialty restaurants, a 6 screen movie theater, an antique and classic automobile collection, various shops, a spa and a fitness center, a swimming pool overlooking the Biloxi Bay, free valet parking, and a 24 hour casino.

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Room Rates:

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NAF will have the top researchers from around the world as well as local doctors and researchers to provide you with the most medical information that you can get specific to the ataxias!

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all, the NAF Conference I saw was attended by four hundred or more ataxic people and their friends. Clearly everything's on a different scale over there – big, brash and American. Organisation of the conference was handled smoothly by NAF Central Office staff, in particular Arnie and Donna Gruetzmacher, whilst the local work was provided by Kay Bell of Huntingdon's Beach and Earl McLaughlin of Orange County respectively.

Structurally the conference itself followed more or less the same format as our own in Europe – medical/scientific reports first in the morning, followed by talks and presentations on what Americans call 'coping with ataxia' and we call 'living with ataxia' in the afternoon sessions. One of the most innovative aspects of the conference were the Sunday Morning workshops. Conference attendees were split into six manageable groups and the resulting degree of informality facilitated lively and engaged discussion.

As far as the scientific papers went nothing really ground-breaking was presented. Still Massimo Pandolfo, MD, gave a very good state-of-the-art report on FA Research: New Perspectives and Developments, while Laurence Schut, MD and Medical Director of the NAF, gave an interesting paper on ataxias which were *not* hereditary.

The afternoon started with a marvellous presentation on service dogs, given for the most part by the dogs themselves, followed by a lecture on coping delivered by psychologist, Stuart Harder. In true American style this was honest and open.

As these conferences often turn out it wasn't really the formal side of the meeting which counted: rather it was very good just to meet people at an informal level.

Yes it was great *cratic* to go to California. The ataxic people in the US are very friendly – though I must admit I found the air journey all the way to LA and back quite dreadful. Next year's conference is being held not just so far away – in Biloxi, Mississippi. Maybe we should try to arrange a contingent from Europe to go overfor it? If so we should start planning soon...

DNA REPEATS

Wim Nas, Carolien Koopmans

Recent scientific research has made clear that many of the hereditary ataxias are caused by repeats of sequences of 3 bases in the DNA of the affected people. Triplet repeats are also the cause of a number of other neurological diseases. The magazine *Scientific American* in its first issue of this year has paid attention to repetitive repeats, so called 'microsatellites'. In the article is suggested that DNA repeats might be the result of the rapid evolution of our brain.

The human genome – some three million bases of DNA – only for a small part (10-15%) consists of genes. The rest, which function is not always clear, is often called 'junk DNA'. Moreover, inside a gene we find coding sequences (exons) and non-coding sequences (introns). We all know that triplet repeats in exons can cause a number of neurological diseases, among which a number of the dominant hereditary ataxias. Even triplet repeats in introns can cause disease as is shown by the example of Friedreich's Ataxia (FRDA). The authors of the article 'DNA Microsatellites: Agents of Evolution' state that "although the only function assigned so far to human microsatellites is negative – causing a variety of neurological diseases –

microsatellites may be surviving relics of evolutionary processes that helped to shape modern humans.”

Bacteria

Bacteria also have genes consisting of DNA. The very high frequency of mutation of some bacteria is discovered to be caused by DNA repeats. The example given in the article is that of *Neisseria gonorrhoeae*, the bacterium that causes the sexually transmitted disease gonorrhoea. In this bacterium some proteins allow it to adhere to and invade epithelial cells and certain phagocytic (bacteria killing) cells of the immune system of the host. Sometimes it is of strategic importance for bacteria to cling to cells (for instance when entering a new host). But at other times, especially in the case of phagocytic cells, it is ‘wiser’ not to do so. By mutating its genes for these proteins from one generation to another, the bacterium can turn its adherence quality ‘off’ or ‘on’. Such genes are called ‘contingency genes’. If only 10 of the 2000 genes of a bacterium are contingency genes the bacterium can produce up to $2^{10} = 1024$ different combinations of genes. This variety enlarges the chance of survival of the bacterium enormously. If only one of the bacteria survives the immune system of the host, it can start a new population of bacteria.

The microsatellites of bacteria surely are evolutionary adaptations. These repeats couldn’t have been retained by mere chance. They have an evolutionary function, because they enable the organism to survive in fast changing circumstances.

Man

The function of DNA repeats in man is largely unclear yet. In the beginning they seemed to have no function at all. Microsatellites in people appeared not to scramble the way DNA is read and not to yield non-functional proteins. But recent research discovered that in

some cases an excessively enlarged microsatellite of three repeats inside a gene leads to the misreading of the gene and therefore to the production of too little protein (as in the case of FRDA) or of a wrong protein (as in the case of some dominant ataxias). Over-repeated triplet microsatellites are also the cause of a number of other neurological diseases, for instance Huntington’s disease.

Evolution

Why do we have microsatellites – which in some cases prove to be genetic time-bombs – inside our bodies? Most of the triplet repeats cause neurological diseases. None of those diseases affect (other) animals. It seems this type of neurological disease is unique for humans. Realising also that neurological diseases concern the Central Nervous System, it is plausible that those degenerative diseases are the price we have to pay for the rapid evolution of our brain. Long microsatellites in or near genes might contribute to the functioning of our CNS and maybe that is the reason why they have persisted throughout human

evolution, even though they occasionally expand too much and cause disease. Maybe microsatellites play a role in the subtle regulation of the brain. Recent research has made clear that microsatellites influence the speed of production of some proteins, among them neurotransmitters. (Neurotransmitters are chemicals that serve as messengers between neighbouring neurons.) Possibly microsatellites function as ‘tuning knobs’ to regulate the amount of protein that is produced. The microsatellites would react to changing circumstances of the cells in the tissue. Microsatellites can regulate the protein production in a more subtle way than by simply switching ‘on’ or ‘off’ the production. This could have had evolutionary profits. Science has only recently started to probe the roles of microsatellites in higher organisms.

[E. Richard Moxon and Christopher Wills, ‘DNA Microsatellites: Agents of Evolution’, *Scientific American*, January 1999, volume 280, number 1, 72-77]

FRIEDREICH’S ATAXIA: NEW DEVELOPMENTS AND PERSPECTIVES

Massimo Pandolfo, M.D., Montreal, Quebec, Canada

Since 1996, Dr. Pandolfo has served as an Adjunct Professor in the Department of Neurology and Neurosurgery and also is Research Associate Professor in the Department of Medicine at McGill University, Montreal, Canada. Dr. Pandolfo, working in collaboration with other researchers, discovered the Friedreich Ataxia gene in 1996.

I will try to summarize where we are in the progress of understanding what causes FA, and to give you some ideas as to what the future direction will be, and what we expect to learn in the next few years.

Professor Nicholas Friedreich, professor of medicine in Heidelberg, Germany first described the disease in 1863. Researchers and

clinicians had a detailed description of the clinical picture of this disease, but did not know the cause, other than it was inherited and recessive. We had no idea what the gene was, what protein the gene coded for, and the reason why people developed symptoms. Finally, in 1996, we identified the FA gene, the segment of DNA containing the genetic information which is abnormal in people who

have the disease.

The gene lies in the 9th chromosome and encodes for a protein called frataxin. The function of frataxin could not be determined at the time the gene was cloned. The first finding, that followed the discovery of the gene, was the understanding of the abnormality at the DNA level. We found the majority of people who have FA carry an unstable trinucleotide repeat expansion, which is an excessive number of repeats of a DNA sequence composed of three of the units (GAA). GAA, instead of being repeated less than 40 times, in a normal chromosome, it was repeated from about 100 to 700 and sometimes more than 1,000 times. Since then, we have learned that an excess number of repeats does not cause the production of an abnormal protein like that which occurs in all of the dominant ataxias, but rather it causes a deficiency of the normal protein. Having too many repeats causes the patients with FA to make a small amount of something that they need in much larger amounts. The size and the amino acid sequence of frataxin is perfectly normal in the patient, but they just have too little of it. This is the consequence of the expansion.

We also realized in the 3 years that followed the discovery of the gene, that this trinucleotide expansion mutation explained at least part of the variability that we see in the clinical picture of FA. The age of onset, the rate of progression, overall severity, and the extent of nervous system involvement for FA may be variable. Some people may have a severe cardiomyopathy, others may have no symptoms of cardiomyopathy at all, some may have problems with vision or hearing, and some may not. Clearly, those individuals that have larger expansions (more GAA triplet repeats within the frataxin gene) tend to develop the disease earlier, and have a

faster progression, which also tends to affect other additional systems. Individuals with large expansions are more likely to have optic atrophy, decreased vision, hearing loss, severe cardiomyopathy, and diabetes. This correlation is highly significant if you do statistical calculations, but it does not allow you to predict the course of the disease in the single patient because there is too much variability. If we do a genetic test and find 700-900 triplets, we cannot say you will come down with the disease at 12 years of age and you will be in a wheelchair at age 25. That is absolutely impossible, because patients with the same number of repeats may have 10-15 years difference in the age of onset and may develop diseases that are quite different in severity. If you look at 200-300 patients you may find a correlation, but in the single individual you cannot make that kind of prediction. This is very important to know and understand.

At this time, we think that expansion sizes can explain 50% of the variation that we see in the disease. The other 50% has to be explained by other genetic factors (other genes that interact with this one), environmental factors that haven't been identified yet, and chance, which plays a role in everything.

The clinical features of FA are even more variable than we thought before. We found individuals who became ataxic at age 40 or 50 and have FA. We used to think of this disease as a disease of children and teenagers. We have people who have very unusual clinical symptoms, like retained reflexes but have spasticity, etc. This has led us to extend this diagnosis to a number of cases that we did not think had Friedreich Ataxia.

Another possible source of variation is the fact that a small number of patients with FA, less than

5%, have a point mutation, a change in the DNA code that causes a change in the protein itself. They have symptoms that are usually typical of FA. It is clear that patients, with a point mutation, have less of the protein, because on one chromosome they have the trinucleotide expansion. They also have some abnormal protein because of the point mutation. They are different from the other FA patients in this respect, but the final consequence is the same.

We have also learned that the FA gene is not equally necessary, or used in all cells of the body. Cells affected by the disease need frataxin in higher amounts than other cells. It is highly expressed in the spinal cord and in the dorsal root ganglia where neurons most severely affected are located. These are the same sensory neurons responsible for position sense, that is very much affected by this disease. The heart is affected by the disease which normally makes a larger amount of frataxin than other cells and tissues in the body. We have to keep this in mind when we try to understand the consequences of frataxin deficiency. Cells make different amounts of frataxin. They are differentially sensitive to a deficiency of frataxin.

The other major finding was what we call the sub-cellular localization of frataxin, which means in what structure within the cell is frataxin localized. We and others have done a number of experiments all confirming that frataxin is made in the mitochondria.

What are mitochondria? They are thousands of little structures within each cell of our body. They are the power house of the cell. Mitochondria are the structures within the cell where a very important chemical reaction takes place, called respiration. This is where the chemical compounds that make up the food that we eat,

are burned to generate energy. Molecules from food and oxygen are combined to produce energy in the mitochondria. Frataxin is localized within the structure that makes energy and essentially burns foods to produce energy.

What is the function of frataxin within the mitochondria? This was a major challenge to understand. It did not look like any protein with known function that had been identified within any living organism. However, what helped was the fact that we realized that all living things make a protein that looks like frataxin: mice, fruitflies, worms, and bakers yeast. Bakers yeast makes a protein that is almost identical to human frataxin, and is localized within the mitochondria of the yeast. The fact that yeast makes a protein identical to frataxin is a great asset because it is easy to genetically manipulate yeast, easier than with mice.

Yeast cells were made, that do not have any frataxin by a number of labs, one of which is Dr. Jerry Kaplan at the University of Utah. The most striking thing that happens with yeast cells without frataxin is the profoundly abnormal iron metabolism. These yeast cells incorporate much more iron than the normal yeast cell and the extra iron incorporated by the cells ends up in the mitochondria. As a consequence of excess iron in mitochondria, cells become highly sensitive to oxidative stress. In the mitochondria, oxygen flows through the protein complexes called the respiratory chain complexes. A small amount of oxygen that is flowing through this complex, in the mitochondrial membrane may form what are called free radicals. This may lead to the formation of H_2O_2 within mitochondria, and H_2O_2 reacts with iron to form the hydroxy radical. The hydroxy radical is a substance which is known to damage mitochondrial proteins, membranes, and DNA. Having too much iron

in mitochondria is something that you do not want to have. After doing this initial study in yeast, it became extremely important to see if we could find anything in human disease that indicated the situation is similar in humans. The current evidence shows that the situation in the human disease is very likely to be the same. The first finding is that if we stain for iron in a tissue section of the heart, from an FA patient, we find iron deposits. This was discovered about 20 years ago by a Canadian neuropathologist. But, at the time there was no way of interpreting the finding until now. In affected tissue, like the heart we see iron deposits like those seen in the yeast model. These iron deposits are found in the heart of patients with FA, but not in the heart of patients that have any other type of heart disease. It is a specific finding. We have an abnormal distribution of iron, too much iron in the mitochondria, and probably too little iron out of the mitochondria, rather than an overall accumulation.

It is interesting to note, that in an old study by a Hungarian neurologist done in the 1960's essentially injected radioactive iron into patients with a variety of neurological diseases. They realized that iron is retained in higher amounts in the brain in patients with FA than in patients with other diseases, or normal individuals. This was another hint that was buried in the medical literature. Something abnormal with iron metabolism was going on with FA. Non-affected tissue, like the skeletal muscle shows no evidence of iron accumulation in this disease. This means that this is a specific process affecting the tissues. Is iron really accumulated in mitochondria? There is recent and exciting data that show that in the hearts of patients with FA there is an accumulation of material that has all the characteristics of iron in the mitochondria, but we do not see this in the mitochondria of the

heart of other people with any other heart disease. It is very specific to FA. We have started to get evidence that iron accumulation in mitochondria does occur in the affected tissue of patients with FA. We are now extending this study to nervous system specimens.

A slight increase in mitochondrial iron can be found in cells that are not affected by the disease like cells from the skin. It is not a big increase, but it has been consistently observed in the mitochondria of the cells. What are the consequences of having too much iron in mitochondria? The specific consequence is that some mitochondrial enzymes that contain iron sulfur centers are inactivated by the excess of iron. This leads to the malfunctioning of the respiratory chain system, and a loss of energy. In addition, this causes the cells to become hypersensitive to oxidants. The cells are dying. What we think is going on is that frataxin deficiency leads to increased mitochondrial iron and this leads to an increased generation of free radicals and mitochondrial damage. On the one hand this leads to energy deprivation, cells do not have enough energy. This may lead to the dying of nerve fibers, in both the peripheral nerves and the spinal cord. On the other hand, mitochondrial damage can directly trigger a process that is called programmed cell death, or cell suicide. This may underlie the cell loss that we see in the heart and other parts of the central nervous system. It is important to say that we have evidence of this process in cell cultures in the lab, but we do not have evidence of this process going on in the living patient. This is a future objective of research.

We would like to have an animal model for FA, and currently there are 7 or 8 different approaches that are being tried to generate a FA mouse model. Hopefully, within a few months or a year this

will be successful.

Secondly, the idea that we have too much iron in mitochondria suggests possible treatments that we can try to slow down the course of the disease. Removing the excess iron is going to be very difficult because the iron is sequestered in the structures where the currently available chelators cannot efficiently penetrate. We can try what are called antioxidants, to buffer some of the free radicals that are produced in the disease. Among the antioxidants used in the test tube, the co-enzyme Q derivatives seem to be the most effective in limiting the toxicity of iron to mitochondrial structures. A number of research groups, like the group in France are trying to test this substance in a controlled study of patients, and we are planning a similar study in Montreal. We don't expect a miracle. At most we expect some slowing down of the disease as suggested by the preliminary data which may be limited and transitory, so don't expect anything. What is important is that even if the first treatment we try does not solve the situation, we have started to gain some understanding of the disease process which in the future will allow us to identify possible targets for drugs that can be tested on patients. This is a major revolution since the gene was cloned.

MY JOURNEYS TO SATHYA SAI BABA

Monika Müller

This year was special for me, marking the 10th anniversary of my journeys to Sai Baba in Puttaparthi, South India.

When I first heard of Sai Baba in a lecture 13 years ago, an old lady doctor told me that by going to him I would do something beneficial, not only for myself but also for my younger sister and brother who were also suffering from Friedreich's Ataxia. Well, when I heard this I didn't need much time to decide and so I booked a trip to Sai Baba that very same evening.

What I learned and experienced in India was so overwhelming that it took me a full four years to allow these new and unfamiliar thoughts to settle in my head: They tell us that we are not separate from God and that people from all religions and cultures are our sisters and brothers.

Sai Baba's teachings helped me to find sense in and give sense to my life; in other words, to take life into my own hands and constantly remain focused on the human values which are the essence and basis of all great religions. These values are truth, right conduct, selfless love, peace and non-violence.

Since 1989, equipped with my own wheelchair, I have been going to see Sai Baba every year. A few times I spent a whole three months in his ashram. Twice I



travelled in a group, but as a rule I am either accompanied by a girl friend or just by myself. But as chance would have it, I actually never found myself alone on these trips, because nearly always I met other Sai Baba devotees with the same goal.

Regarding the doctor's 'prophecies', my trips remained without effect on my sister's and brother's condition. As a matter of fact, my brother died already ten years ago and my sister's present physical as well as mental state is quite poor. But for me, the course of the disease is rather mild. Now at the age of 46, I still manage to get along *on my own*, although with considerable difficulty, but nevertheless on my own. I still work in my profession and am – in addition to that – always engaged in one or another interesting project; perhaps, because I find it hard to say 'no'. At present, I am sounding out my theatrical abilities and have thereby discovered that acting is fun! I am making a monthly radio programme for disabled as well as non-disabled people, and on TV I am moderating an information programme for the disabled community. And last but not least, I have recently began to try my talent as a fashion model – in my wheelchair.

My mother is happy about my journeys to Sai Baba. She knows only too well how much they mean to me and what invigorating and uplifting effect they have on me. Besides, the warm Indian climate has a soothing effect on my body. My grandmother feels the same

way, since she noticed the change in me which my connection to Sai Baba has brought about. I am fully aware now of what is important in life and live up to my truth.

Three times I was fortunate enough to have an interview with Sai Baba. To have an interview means to be invited into a private room, together with a small group, where he speaks about spiritual matters to those present and also replies to their personal questions and problems. In my first interview I asked him, whether there was any remedy against FA. Three times he said ‘yes, yes, yes’ and materialised a *lingam* for me. A lingam which is of oval shape (like an egg) is symbolic for the process of creation. Both the atom and the planetary system are of elliptical shape. The materialisation of objects out of nothing is certainly God’s great miracle, but the greatest miracle is his infinite love and compassion, which I had the good fortune to experience myself. In my first interview Sai Baba encouraged me to get up from my wheelchair, which I was able to do in his presence with the support of his arm. For me this was an absolute divine experience. There was no pain whatsoever and yet I was able to feel each cell in my body. I expressed the desire to walk around my wheel chair, but under the effort I kind of panicked thinking ‘it is not possible’ and reached out for my wheelchair again. The same thing happened on the occasion of my third interview. Just when I was supposed to cross the tiny threshold of the door leading to the interview room, fear seized me and made me call for the wheelchair.

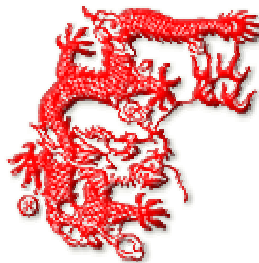
Now, I am taking a good look at my fear and inner blockades, for I realise only too well that that part in me which is still rigid will have to be transformed, so that I may turn to the divinity within. Divinity is equally present in all of us, and it is only up to me/us to real-

ise it. Once we have taken this step, divinity can flow freely and allow us to experience peace and happiness.

ENTER THE DRAGON

Peter Bayliss

Like many ataxic and other similarly neurologically impaired people, the deterioration in my handwriting first meant an increasing reliance on a typewriter for letters and all other written work. From the typewriter, I moved on to the first of several computers, which over the years have become more powerful and sophisticated. But, like the typewriter, they relied on a keyboard and so required the same basic typing skills. My two-finger typing was never very fast or accurate at the best of times, and it inevitably deteriorated as time went by. This prompted me to look at the possibilities of voice recognition for my computer.



I had seen DragonDictate being demonstrated on a visit to the Computability Centre, Warwick. Although there are many such voice recognition programs on the market nowadays, Dragon was the first and is still regarded as being the best. I next arranged for the Centre to give me an assessment. This was really essential – apart from assessing my ability, it also gave me a valuable opportunity for some hands-on experience.

I discovered one of the advantages of DragonDictate is that it’s not just for dictation, but can command any of the computer’s functions in Windows, including mouse pointer movement and

double-clicking. In fact, it gives you complete hands-free use of the computer. Another major advantage is that you save your ‘user’ file after every session. This is particularly useful for ataxians and others with progressive disabilities, since it means that any deterioration in your voice is taken into account as you go along.

In the beginning, ataxians may be concerned about their voices not being good enough for voice recognition. This worried me a bit to start with. But the system responds to certain sounds rather than to voice clarity, so it isn’t at all necessary to be clearly-spoken. When you first get Dragon, you go through a training session which associates the sound of your voice with particular words. Anyway, a fellow FAer who uses it reckons it helps to improve your speech by making you more aware of the way you pronounce words, and so provides an element of speech therapy. Though, as I’ve said, clarity is not essential to Dragon’s recognition of the words. The speech therapy element is an added bonus.

When there are several possibilities for the same word (bough/bow, tale/tail, way/weigh, there/their) a little menu pops up on the screen so you can choose which one you want – you say “choose 2”, “choose 5”, etc. Certain words, especially proper names, need to be spelt out. To allow you to do this, part of the initial training involves Dragon learning to identify your voice with each letter of the alphabet, “alpha, bravo, charlie, delta” and so on. Words which it otherwise doesn’t recognise can also be spelt out, either directly onto the screen or else in the menu – you say “spell mode”, then “choose 1” to substitute the correct word. And you can erase mistakes by saying “scratch that” – it usually comes out something like “scaach’at” when I say it, but Dragon usually understands me. The microphone is extremely sensitive – you need to

adjust the headset so it's only a finger-space away from your mouth. Deep breathing can sometimes mistakenly produce a word, and if you swear after making a mistake, then you have to make sure the swear words do not appear in your finished work!

When I first saw Dragon being demonstrated, one thing which fascinated me (and still does) is that it recognises long and difficult words like "accessibility, necessarily, approximately", words which would otherwise have taken me a long time to type out. And it automatically gets the spelling correct, so I no longer need to run the spell check. You might point out that these words are difficult enough to say. But remember that Dragon responds to the sounds rather than the exact pronunciation, and if you spell the word in the "spell mode" Dialogue Box, you only need to pronounce the first few letters and Dragon will automatically fill in the rest of the word. I realise all this begins to sound very complicated, but believe me you soon pick it up.

In recent years, the price has fallen dramatically. Only a few years ago, the cost was several hundred pounds. But I've recently upgraded my version at a fraction of that amount. However, when the system is initially installed, you will have to pay extra to get the microphone and additional little bits of hardware fitted. My upgrade came from the Speech & Training Company Ltd., the sole UK agents. But there are many retail outlets in the UK who will fit Dragon under licence and provide the necessary training. There are similar arrangements in other European countries (details of Dragon's European offices are given below).

Dragon has launched 'NaturallySpeaking', a version which allows people to dictate in a more natural and flowing fashion instead of pausing after every word as one is recommended to do in the other versions. I think one needs to be very cautious about this. People with FA and others who are similarly disabled tend to speak in a rather staccato manner. NaturallySpeaking does not therefore have the advantages that it has for people without these problems. Whether or not this other system would be of benefit is very much a personal matter. In my own experience, no two people with FA are identical in their symptoms, and problems with speech vary a lot. The Speech & Training Company have pioneered a program called SpeakEzi to be used in conjunction with Dragon. This is designed especially for those with severe speech difficulties, but I think one needs an independent assessment before deciding on this.

Voice recognition has been a life-saver for me, and I would strongly recommend it to other ataxians. Of course, I can only speak about DragonDictate, and there are many other systems. But as I have mentioned above, Dragon is the oldest and most reliable. It is also available within the major European countries and in various different languages. A list of world-wide resellers is available on their Internet website (see URL address below).

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CLOSING DATE

FOR THE NEXT

ISSUE

1 DECEMBER 1999

EURO-ATAXIA 11TH ANNUAL GENERAL MEETING, 29 – 31 OCTOBER 1999

The 1999 Annual General Meeting will be held in Westende (Belgium) from 29 – 31 October. On the same occasion EURO-ATAXIA, together with the Fondation de l'Ataxie Cérébelleuse (FAC), will organise a

INTERNATIONAL CONGRESS ON CEREBELLAR ATAXIAS

We hope you will join us in this attractive meeting, which includes scientific sessions with prominent scientists in the field of cerebellar ataxias.

For more information, please contact EURO-ATAXIA's Secretary-General **before 29 August**:

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The meeting will take place in:

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PROGRAMME

Friday, 29 October

16.00 – 22.00: Arrival and Registration

Saturday, 30 October

Scientific Meeting

07.30 – 10.00: Registration

09.30 – 10.00: M. Manto & D. Kroebel
Introduction

Session 1. Chair: J. Jacquy, President of the FAC

10.00 – 10.15: H. Topka, Tübingen, Germany
Pathophysiology Of Cerebellar Ataxia

10.20 – 10.35: M. Gomez Beldarrain, Galdakao, Spain
Cerebellum And Cognition

10.40 – 10.55: T. Brandt, Heidelberg, Germany
Stroke In Posterior Fossa

11.00 – 11.15: D. Gangji, Brussels, Belgium
Paraneoplastic Cerebellar Syndrome

11.20 – 11.35: P. Seeldrayers, Charleroi, Belgium
Cerebellar Involvement In Multiple Sclerosis

11.40 – 11.55: T. Klockgether, Bonn, Germany
Sporadic Ataxia In Adults

12.00 – 13.40: Lunch

Session 2. Chair: E. Brunt, Vice-President of Euro-Ataxia

13.40 – 13.55: B. Vernet-Der Garabedian, Paris, France
Animal Models Of Cerebellar Ataxias

14.00 – 14.15: S. Dethy, La Louvière, Belgium
Effects Of Toxics On Neurotransmission In Cerebellum

14.20 – 14.35: J.J. Martin, Antwerpen, Belgium
Cerebellar Ataxia In Ceroid Lipofuscinosis

14.40 – 14.55: A. Verrips, Nijmegen, The Netherlands
Cerebrotendinous Xanthomatosis

15.00 – 15.15: P. Cras, Antwerpen, Belgium
Neuropathology Of Familial Prion Diseases

15.20 – 16.00: Coffee Break

Session 3. Chair: M. Koenig, President of Euro-Ataxia

16.00 – 16.15: E. Brunt, Groningen, The Netherlands
Familial Episodic Ataxias

16.20 – 16.35: M. Koenig, Strasbourg, France
Isolated Vitamin E Deficit

16.40 – 16.55: A. Durr, Paris, France
Clinical And Molecular Aspects In Autosomal Dominant
Cerebellar Ataxias

17.00 – 17.15: L. Van Maldergem, Loverval, Belgium
Pitfalls In The Diagnosis Of Trinucleotid Expansions

17.20 – 17.35: F. Kreuz, Dresden, Germany
Advances In Genetics Of Ataxias: An Overview

17.40 – 18.00: J.J. Cassiman, Leuven, Belgium
Impact Of The Commission Projects On The Future
Medicine And Public Perception Of Research

18.00 – 18.10: M. Manto
Conclusions

Saturday Evening

20.00 –: Come Together in The Cafeteria of Zon
En Zee

Sunday, 31 October

Business Meeting of EURO-ATAXIA

9.00: Opening of the Meeting by the President, Michel
Koenig.

- News in recessive hereditary ataxias, Michel Koenig
- News in dominant hereditary ataxias, Ewout Brunt

- Report of the Secretary – vote
- Report of the Treasurer – vote

- Election of the President – vote
- Election of the Board – vote

- New members

- The Newsletter
- The Scientific Board
- Varia

12.00: End of the Meeting

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