

Brain Research UK



Our vision is a world where everyone with a neurological condition lives better, longer

The brain is the most complex organ in our body. It weighs just 3lb, yet it controls our emotions, senses and actions, every single one of them. It is how we process the world around us. So when it breaks down, we break down.

It doesn't have to be this way.

There are hundreds of neurological conditions. We fund research to discover the causes, develop new treatments and improve the lives of those affected.

Let's unite to accelerate the progress of brain research. Today.



1 in 6 of us
has a neurological condition



More under 40s
are killed by brain tumours than by any other cancer



Every 90 seconds
someone is admitted to hospital with a brain injury



190,000
migraine attacks occur every day

*The figures shown relate to the UK

Welcome to our Annual Review



One in six of us has a neurological condition.

Brain Research UK is the leading dedicated funder of neurological research in the UK. We fund the best science to achieve the greatest impact for people affected by neurological conditions, to help them live better, longer.

Throughout the year, despite the challenges of Covid-19, our supporters were inspiring and humbling as they committed to raising funds. The pandemic elicited a range of creative fundraising activities and extraordinary enthusiasm, enabling us to fund vital neurological research.

I am delighted to report that, thanks to these extraordinary efforts, we were able to award more funding than originally anticipated. We continued to fund in our three priority areas of brain tumours, brain and spinal cord injury, and headache and facial pain through the award of three new PhD studentships and four new project grants. We also funded the first two Brain Research UK Miriam Marks Fellowships for research into neurodegenerative diseases and awarded a new joint fellowship with the Royal College of Surgeons.

As well as the above funding awards, totalling £2,002,524, it became clear that our existing grant-holders would need additional time and resources to complete their projects. We remain fully committed to these projects and awarded £140,632 of extension funding to ensure they could deliver on their original objectives.

There is no question that it has been a difficult year for us all. Our thanks go not only to our supporters but also to our many grant-holders who have worked so hard to keep their projects on track. I also extend our thanks to the members of our Scientific Advisory Panel for the time and effort they have contributed, despite dealing with the impact of Covid-19 on their own work, as well as to the many reviewers who took time to assess funding proposals to help ensure that the very best research continued to be funded.

In the following pages, we feature some stories from our many valued supporters. We receive no government funding and it is only thanks to our valued supporters that we are able to fund the life-changing, life-saving research highlighted in this review.

It is difficult to find adequate words to express our debt of gratitude to all those who so kindly support our work, especially with all that has been endured during this year. My sincere thanks to all who help to progress neurological research. I look forward to all we can continue to achieve together in the future.

Jim Gollan
Chair of Trustees

Covid-19: Research and fundraising impact



In April 2020, the UK was in lockdown and Covid-19 was spreading quickly throughout the country. Normal life was grinding to a halt.

Research is suspended

Like other workplaces up and down the country, research laboratories had been forced to close their doors. Clinical research taking place in hospitals and other settings was suspended.

As we closed the doors to our own office and set up desks at home, we began to contemplate the impact of this interruption to our research projects. It was clear that research teams were going to need additional time to complete their planned research, but how would this be funded? Who was going to pay salaries and stipends during lockdown? What costs would be incurred as a result of experiments being abandoned and then re-started? The costs were mounting at a time when income was shrinking.

Despite initial uncertainty about whether charity-funded researchers were eligible for furlough, most of the salaried research staff on our grants were eventually furloughed by their research institutes. PhD students were not eligible, so we continued to pay their stipends throughout. Once labs reopened, and clinical research was able to resume, staff returned to work but ongoing restrictions and social distancing requirements meant that most were unable to work at full capacity for many months. In some cases, the abandonment of experiments meant the loss of months' worth of work, which had to be repeated.

Our commitment

All the research we fund has been chosen because of its potential to deliver benefit for people with neurological conditions. We had already invested millions of pounds in these projects and it was obvious that we needed to ensure that the projects were able to recover and deliver on their original objectives. We worked with our grant-holders to assess the extent of disruption to their research, and determine what additional resources were required. During the year, we awarded a total of £140,632 for Covid-related extensions and expect that we will need to find a further £60,000 next year.

In light of the crisis in medical research funding, and despite our reduced income, we took the decision to proceed with our annual project grant round in order to maintain momentum in our three priority research areas: brain tumours, brain and spinal cord injury, and headache and facial pain. We awarded four new grants totalling £1,086,425 in September 2020; details of the funded projects are provided within the pages of this review.

In March 2021, and with our commitment resolute, we awarded three, rather than the usual two, PhD studentships totalling £348,230. Again, details of these studentships are provided on the following pages.

Impact on fundraising

Like so many charities, we rely on fundraised income to support our work. The London Marathon is particularly important to us, with our incredible runners generating more than a quarter of our annual donated income. The 2020 event had been due to take place just weeks after we went into the first lockdown, and our team was on track to raise £600,000. Postponed, then cancelled, and with the 2021 event taking place in October rather than the usual April, it played havoc with both training and fundraising. We are grateful beyond words to our fantastic runners, whose loyalty and enthusiasm remains undiminished.

Whilst the London Marathon was one of the first fundraising events to be cancelled, many others followed. From other high profile events such as the Great North Run to local runs, walks, bake sales and concerts, fundraising was paused. The 2.6 Challenge was born, encouraging people to raise money for charity by doing 2.6 of something – anything – on London Marathon day and beyond.

We are hugely grateful to all those who raised money for us throughout this difficult year. It is only thanks to the determination and ingenuity of our supporters that we received donated income of £1,383,000, almost 75% of what we had hoped before the pandemic, and with much of the shortfall being a result of the cancellation of the London Marathon.

The road to recovery

It is clear that we will be dealing with the impact of Covid-19 for many years, on a scale that is difficult to comprehend. From the personal struggles of those who have been severely ill with Covid-19, those who have been bereaved, have lost jobs or whose businesses may have closed, to the broader effects on society and way of life. The NHS and the medical research sector will take years to recover lost ground.

Brain Research UK has a small, dedicated staff team and low overhead costs. We will continue to work hard, to do our very best to weather this storm and overcome the impact of Covid-19, so that we can continue to fund research to help everyone with a neurological condition live better, longer.

Your support makes a world of difference.

"After the most challenging of years, we look back with pride and offer heartfelt thanks to all our stakeholders – supporters, researchers and volunteers – who made an exceptional contribution and worked tirelessly to ensure that vital neurological research could continue. Thank you. We now look forward to how much more can be achieved, together."

Caroline Blakely
Chief Executive



Our strategy



Our vision is a world where everyone with a neurological condition lives better, longer.

As a result of the global pandemic, like many other organisations, we faced a disrupted and fragmented 2020/21. However, Brain Research UK was well positioned to fulfil its objects and to improve the lives of those affected by one of hundreds of neurological conditions, through the funding of essential research and accelerating its progress.

Our strategy remains focused on how we can have a greater impact on those living with a neurological condition through the funding of more research, underpinned by stable, secure financial foundations. Key highlights of our strategy are summarised below.

Research

We will continue to fund world class, impactful neurological research.

Within this broad remit of neurological research, our aim is to focus our funding in areas where research investment is most urgently needed. Since 2016, our focus has been on research into brain tumours, brain and spinal cord injury, and headache and facial pain. In each of these three areas, there is a large unmet patient need that is not reflected in current levels of research funding.

Brain tumours

- 12,100 people are diagnosed with a primary brain tumour every year in the UK, and 5,400 lives are lost.
- Brain tumours are difficult to diagnose and treat. We want to improve the outlook for those affected by funding research that takes forward our understanding of the mechanisms underlying tumour development, and helps develop better ways to diagnose and treat these tumours.

Brain and spinal cord injury

- At least 2 million people in the UK are living with disabilities caused by an acquired brain or spinal cord injury. This includes both traumatic injuries, caused by an accident or external injury, and non-traumatic injuries, such as those caused by stroke.
- We want to improve understanding of how to repair the brain and spinal cord after injury, to help people make a better recovery.

Headache and facial pain

- Headache has been described as the most common medical complaint known to man and, because of its prevalence, is one of the leading causes of disability.
- There are hundreds of different types of headache and facial pain disorders, including migraine and cluster headache. We want to improve people's lives by funding research that addresses the causes and mechanisms of these disorders, and advances diagnosis and treatment.



We will continue to review our priority areas on an annual basis.

We will continue our two national funding schemes through which we offer project grants and PhD studentships in our priority areas. Over the next two years, we aim to fund a minimum of four studentships and six project grants and we will collaborate with other funders and charitable organisations to maximise research impact.

Collaboration

We will work collaboratively, across both fund-seeking and grant-making activities, with like-minded organisations with shared purpose.

Communications

We will diversify our communications activities to ensure that we retain existing, and attract new, supporters.

Fundraising

We will focus on developing our existing flagship fundraising streams, such as the London Marathon, and will seek to grow sustainable income from major donor and corporate fundraising channels.

Organisation

In order to achieve the strategic goals outlined above, we will continue to monitor, and where necessary improve, our working practices and the way we work.

We will focus on being a lean, agile, modern and adaptable organisation that can mobilise and respond quickly to changing circumstances.

Our key aim is to maximise fundraising income while keeping our operational costs low in order to fund essential research and accelerate its progress – ultimately making positive change for our beneficiaries and helping to realise our vision of a world where everyone with a neurological condition lives better, longer.

Our research



Our charitable objects allow us to fund research into all types of neurological condition. This is a broad remit, within which some disease areas have a higher profile and a higher level of research funding than others.

Following a review in 2016, we identified three disease areas where there is a particular disparity between the level of unmet need and the level of current research investment: brain tumours, brain and spinal cord injury, and headache and facial pain.

We continue to prioritise these three areas, focusing our funding on research that will help unravel the underlying mechanisms of these conditions, and aid the development of new diagnostic and treatment approaches. In this way, we hope to achieve maximum impact with the funds available to us.

How we fund

We fund research in these areas through two national schemes: project grants and PhD studentships. Both of these schemes are popular and attract a growing number of high quality applications every year.

Awards are made following a rigorous assessment process that involves review by relevant external experts as well as our own Scientific Advisory Panel. In this way we can be sure that we are funding high quality research that is most likely to deliver results for those affected by these conditions.

Despite the disruptions caused by the pandemic, we were able to deliver both of these schemes and funded four exciting new projects and three promising PhD students during the year. Information about these awards can be found on the following pages.

Building research capacity

A key component of our research strategy is our investment in the future of brain research, to build capacity in underfunded areas.

It is crucial that funding is available for junior researchers, not only to attract them into the field, but to keep them there.

Our PhD studentships are key to our strategy of capacity building. Since 2016, we have funded 11 studentships in our three priority areas. These studentships have gone to outstanding candidates, passionate about research in the field that they have chosen, and we anticipate that each will make a lasting and valuable contribution to research in these fields.

We also have a focus on Early Career Researchers (ECRs), defined as those with less than 10 years since PhD, and encourage the submission of project grant applications from those in this category. Three out of the four project grants awarded this year went to ECRs.

In addition, this year we funded our first joint fellowship with the Royal College of Surgeons. Their Surgical Research Fellowships offer junior trainee surgeons the opportunity to obtain research training, providing one year's salary and some research costs. We co-funded neurosurgical trainee Yizhou Wan, whose research in cognition and glioblastoma is outlined on page 13.

Endowment funding

When Brain Research Trust was founded in 1971, it was to support the development of a multi-disciplinary basic research programme at the Institute of Neurology, to complement and underpin the clinical research being carried out at the two Institute hospitals: the National Hospital for Neurology and Neurosurgery, and University College London Hospital. It was anticipated that this would attract scientists from all over the world and encourage cross-fertilisation of ideas. Generous founding donations were received from, amongst others, the Miriam Marks Charitable Trust and the Anne and Michael Sobell Charitable Trust.

These donations were endowed to support the establishment of the Department of Neurochemistry, and a Chair in Neurophysiology respectively. Since the 1970s, these Departments have flourished and have evolved to keep pace with changes in research groupings that have gone hand in hand with advances in knowledge and technology. Through the endowments, we continue to support their work.

The aim of the Miriam Marks endowment was to support research in neurodegeneration, in memory of Mrs Miriam Marks who died with Alzheimer's disease in 1971. The endowment has supported a wealth of research over the years and in 2020 we were pleased to launch the Brain Research UK Miriam Marks Fellowships to support researchers focused on neurodegenerative diseases. During the year, we awarded the first two Fellowships to Professor Antonella Spinazzola and Dr Jonathan Rohrer; their work is outlined on pages 20 to 21.



The past year has been such an important one for medical research. The astonishing speed with which scientists have developed, tested and rolled out coronavirus vaccines has demonstrated what can be

achieved when the right resources are available. At the same time, scientists and doctors have worked side by side to test new approaches to the treatment of patients seriously ill with Covid-19. This research has saved so many lives, and has given us a path out of the pandemic. All of this underlines the huge importance of medical research, and of having a robust, well-resourced research infrastructure that is equipped to tackle not only emergent problems such as Covid-19, but also the diseases of old that still have no cure.

Medical research has been badly disrupted by the pandemic, however, with swathes of research grinding to a halt during the first lockdown and many restrictions still in place. A decline in charity funding, caused by loss of income during the pandemic, puts ongoing and future research at risk.

We continue to receive many high quality applications under our two national funding calls. The research described on the pages of this report came highly recommended by the Panel, the best of two strong rounds of applications, and we look forward to following the progress of the respective teams.

Professor Kevin Talbot MB BS, DPhil, FRCP
Nuffield Department of Clinical Neurosciences,
University of Oxford
Chair, Scientific Advisory Panel, Brain Research UK



Brain tumours

Every year in the UK, more than 5,000 lives are lost to brain tumours.

Compared with other types of cancer, a disproportionate number of these deaths occur in younger people: brain tumours kill more people under 40 than any other cancer.

With more than 130 different types of brain tumour, which may all present with different types of symptoms, they are difficult to diagnose and exceptionally difficult to treat. Survival rates vary widely between the different types of tumour but, overall, only 40% of adult patients survive one year from diagnosis and only 12% survive five years.

Brain tumour research receives a disproportionately low share of research funding, and this has hindered progress. It is clear to see how sustained investment in research into cancers such as breast cancer, prostate cancer and leukaemia has transformed the outlook for patients.

This is why we are prioritising research into brain tumours. We want to improve survival in people with brain tumours by funding research that advances understanding of the mechanisms underlying tumour development, and helps develop better ways to diagnose and treat these tumours.

Funding research into brain tumours

Thanks to the support of people like the Beal family, featured opposite, we have invested £1.8 million in brain tumour research since 2016, when we made this area a research priority. We are funding research that is helping to advance understanding of how and why brain tumours arise, and providing greater insight into how they can be treated both effectively and safely.



This year, we awarded grants for one PhD studentship, three new projects and one neurosurgical fellowship focused on brain tumours. The work being carried out under each of these five awards promises to make an important contribution to knowledge and, crucially, to translate to real benefit for patients.

▼ Phage-guided therapy in paediatric medulloblastoma



PhD student **Lauren Gay** is working on the development of a new treatment approach for medulloblastoma, the most common brain cancer in children.

Advances in treatment have increased survival from medulloblastoma but

current treatments, whilst potentially life-saving, have an unacceptably high risk of life-altering side effects.

Working with supervisor Professor Amin Hajitou at Imperial College London, Lauren is working on an alternative, safer treatment approach that could save lives without harming the developing brain.

She will use a harmless virus, known as a bacteriophage, as a carrier to deliver a therapy directly to tumour cells, aiming to destroy these cells whilst sparing healthy tissue. She hopes to demonstrate that this type of tumour-targeted therapy has the potential to replace current invasive and toxic treatments, with scope to improve not only survival but also quality of survival.



▼ Bartholomew's story An incredible talent, a life cut tragically short



We are indebted to the family of Bartholomew Beal for the wonderful support they have given over the last year. Barley, a talented professional figurative artist, sadly died, aged 30, in December 2019 from an astrocytoma, a brain tumour. Despite living with the tumour for nine years, Barley had extraordinary zest and energy, hurling himself at every

opportunity with indifference to his condition. Such was his approach to life that many, even those he worked with closely, had no awareness of his circumstances.

Barley's work habitually grew out of literature. Solitary figures, often aging and bearded, were to be found in indeterminate surroundings, amid over-arching giant vegetation or floating images suggestive of a life full of colours.

In August, on the anniversary of what would have been Barley's 31st birthday, his family made the decision to produce and sell 75 limited edition prints of his painting, 'The Fool's Marotte', with all proceeds donated to the charity. In March, following this hugely successful sale, his family arranged a second limited edition sale of 75 prints of his painting, 'Ash on an old man's sleeve', again with all proceeds donated to us. Such was the popularity of Barley's work, the prints sold in under an hour on both occasions and collectively raised an impressive £38,500.



The Fool's Marotte, by Bartholomew Beal
45 x 25 cm, Oil on Canvas, 2015



Brain tumours



▼ A new combination therapy for glioblastoma



Professor Khuloud Al-Jamal and colleagues at King's College London are designing a new treatment for glioblastoma, the most common primary brain cancer in adults.

This deadly tumour has no treatment that is effective in the long-term,

and only a quarter of patients survive more than a year from diagnosis.

Addressing the desperate need for effective treatments for glioblastoma, Professor Al-Jamal aims to develop a new treatment that combines chemotherapy and immunotherapy techniques.

Her research will tackle one of the major obstacles to successful treatment of brain tumours – the blood-brain barrier (BBB), which hampers delivery of drugs to the brain. Key to the success of this project is a delivery mechanism to ensure that their new treatment can bypass the BBB and reach cancer cells at high concentration. To achieve this, they will use nanocarriers 10,000 times smaller than a human hair to deliver the treatment to the tumour.

Following conclusion of this work, Professor Al-Jamal will be poised to take the new treatment through to clinical trial.

▼ Towards precision therapy for diffuse midline gliomas



Dr Manav Pathania and colleagues at the University of Cambridge are studying diffuse midline glioma (DMG), an aggressive and incurable childhood brain tumour.

The nature and location of these tumours means that surgical removal

is rarely possible, and there are no curative therapies. Most children die within 18 months of diagnosis.

New treatments for DMG are urgently needed.

Dr Pathania's team is studying the genetic mutations most commonly found in these tumours, to determine their roles in tumour growth. He is focused on a mutation in a gene called *ATRX* and wants to understand how *ATRX* mutations co-operate with mutations in other genes to allow tumour cells to grow and divide.

He will test drugs designed to counteract the processes that are set in motion by these mutations, to see whether this can reduce tumours.

The ultimate goal is the development of a targeted, patient-matched approach to treating DMG that will eradicate the tumour without causing unnecessary damage to young, developing brains.

▼ Understanding the margin zone in brain cancer



Neurosurgeon **Mr Ryan Mathew** brings together a collaborative team from the Universities of Leeds, Nottingham and York to tackle the problematic cancer cells that remain in the so-called 'margin zone' following brain tumour surgery.

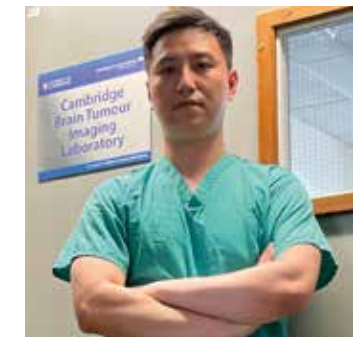
One of the main barriers to successful treatment of brain cancer is that the tumours do not have a clean boundary as they infiltrate the surrounding healthy brain. This means that cancer cells are left behind after surgery, in a margin zone that comprises both cancer cells and healthy brain tissue.

The cells in this margin zone are the root of relapse and being able to eliminate them holds the key to treatment that is most likely to be successful in the long-term. However, very little is known about the way that the cells in the margin zone behave, as most research has focused on the main lump.

This collaborative team is developing new tools to enable the study of the margin zone cells in a living system and work on better ways to eliminate them.

This will accelerate the development of effective treatments for these devastating tumours.

▼ Predicting postoperative cognition in glioblastoma



As part of an important new collaboration with the Royal College of Surgeons, neurosurgeon **Mr Yizhou Wan** was awarded the first ever joint Brain Research UK – Royal College of Surgeons Fellowship.

Mr Wan's research focuses on glioblastoma, specifically the cognitive problems experienced by patients. At least half of those with glioblastoma will suffer from increased problems with memory, planning and concentration following surgery. This has a huge impact on quality of life as well as reducing survival.

Surgery is challenging because these tumours spread into the healthy brain. Surgery involves a delicate balancing of risk between removing as much tumour as possible, to improve survival, versus not causing harm by damaging healthy tissue.

In this one-year fellowship, Mr Wan is using magnetic resonance imaging (MRI) to investigate the effects of tumour and surgery on cognition. His aim is to enable neurosurgeons to preoperatively predict the likely effects of tumour surgery, and thus help understand what parts of the brain cannot be resected without causing a deterioration in cognitive function and survival.





Brain and spinal cord injury

Advances in emergency care mean that many more people now survive serious brain and spinal cord injuries. As such, there are many people living with the long-term effects of these injuries.

The degree of impairment varies enormously but many people are left severely disabled and need long-term rehabilitation to maximise function, independence and quality of life.

We have highlighted brain and spinal cord injury as an area in need of increased research investment. We are funding research to help understand how to repair the brain and spinal cord, to help people make the best recovery from their injury – whether this is being able to walk again, use their arms, communicate, or recover senses or memory.

Funding research into brain and spinal cord injury

Since making brain and spinal cord injury a research priority in 2016, and thanks to the remarkable support of people like Jessie (featured opposite), we have invested more than £2.6 million in research to help us understand how to repair the brain and spinal cord following injury.

This year, we awarded a PhD studentship to Isobel Chick, a speech and language therapist who previously worked with adults with acquired neurological conditions including stroke and traumatic brain injury. Communication difficulties can have a devastating impact on quality of life, and Isobel's research aims to develop a more personalised speech and language therapy intervention to aid communication.



▼ The role of multimodal cues in aphasia



Speech and language therapist **Isobel Chick** is well aware how debilitating communication difficulties, known as aphasia, can be.

"Through my work with adults with acquired brain injuries, I have become increasingly aware of the negative impact that

impaired communication has on quality of life, ability to return to work and to engage in everyday relationships and, consequently, the vital importance of generating effective, timely and person-centred therapy programmes."

Working with supervisor Professor Gabriella Vigliocco at University College London, Isobel is focusing on the non-speech aspects of communication – such as pointing and gestures – known as multimodal cues. These cues are useful in everyday communication, and Isobel proposes that people with aphasia could benefit from using them to communicate more effectively.

In order to develop personalised speech and language therapy (SLT) interventions that incorporate the use of multimodal cues, Isobel first needs to understand how people with aphasia understand and use multimodal cues, and the differences in communication between people with damage to different parts of their brain. She will then proceed to design and trial a personalised SLT intervention to help people understand conversations and retrieve words more easily. This should lead to significant improvement in their ability to communicate and, consequently, their quality of life.

► Jessie's story

In 2015, whilst on holiday in South Africa, Jessie suffered a traumatic brain injury. She unexpectedly passed out, which caused her to fall to the floor and hit the back of her head on the corner of a tiled step. No one knows why Jessie passed out when she did and it had never happened before.

The accident caused a subdural haematoma – an accumulation of blood between the brain and skull. With nowhere to go, the accumulating blood puts pressure on the brain, causing life-threatening damage.

Jessie was a Glasgow Coma Scale 3 when she arrived at hospital; this is the lowest possible score and is associated with a slim chance of survival. She had surgery to drain the bleed and was put in an induced coma. Whilst in the coma she suffered a further bleed that led to more surgery.

Jessie was in a coma for three weeks in South Africa but, against the odds, she regained consciousness and was able to fly back to the UK eight weeks later. During a year of rehabilitation, she had to re-learn how to do simple tasks, including walking and feeding herself. Jessie recalls how difficult this was:

"I was lucky enough to make a full recovery and have no lasting effects but I would say my injury has changed me as a person. Whether that's because the injury to my brain has caused a slight personality change or it is just living through an experience like that, I'll never know."



This period in Jessie's life has taught her a lot but, mainly, that there is so much about the brain that we do not know, which is why she is keen to raise awareness of the need for research. She now has a three-year old daughter and wants to ensure that she grows up knowing her mum's story and knowing that anything is possible.

In October 2020, Jessie took part in the Virtual London Marathon and ran 26.2 miles over the course of 24 hours, raising almost £3,000.

"I have a real connection with Brain Research UK and understand the importance of research funded by the charity. If research could not be undertaken, my story could be very different."





Headache and facial pain

Headaches are extremely common, nearly everyone has one occasionally. When they occur repeatedly, they are a symptom of a headache disorder. More than 20 million people in the UK, two in five adults, are affected by a headache or facial pain disorder.

Primary headache disorders include migraine, tension-type headache and cluster headache. These range in frequency and severity. Due to their prevalence, headaches are one of the leading causes of disability, responsible for three quarters of all neurological-related disability.

New treatment approaches are desperately needed, but a lack of research investment has hampered progress. This is why we are prioritising research into headache and facial pain.

We want to improve people's lives by funding research that addresses the causes and mechanisms of headache and facial pain, and advances diagnosis and treatment of these disorders.

Funding research into headache and facial pain

Since making headache and facial pain one of our research priorities in 2016, and thanks to people like Marleen (featured opposite), we have invested more than £1 million in much-needed research to advance understanding of these disorders and how to treat them.

This year, we have awarded two new grants in headache and facial pain: to sleep researcher Dr Megan Crawford at the University of Strathclyde, and PhD student Clarissa Rocca at UCL Queen Square Institute of Neurology. Their projects are featured overleaf.



▼ Marleen's story



Marleen has suffered from migraine for around 18 years, and describes what it's like to live with the condition.

"I have chronic migraine, so have a headache most days. I get an intense pain

on one side of my head, this can be throbbing or very diffuse but intense pain, or the feeling that knives are being wedged into my brain. I am often nauseous but rarely vomit. I feel utterly exhausted when I am going to get a migraine, or for days after I've had one. Sometimes I feel very depressed for no reason for a couple of hours, after which a massive migraine kicks in. Very weird. I cannot think of words and am confused and unable to focus on things when I have an attack. I am not a person who goes to bed when I have an attack, but I am very restless and do random things. But mostly I have such a headache that sometimes I don't see the point of anything anymore."

Marleen has learned how to adapt her life to avoid some of the things that trigger migraine. Coffee and alcohol are triggers, and she has to avoid getting too hungry and thirsty. Lack of sleep is also a trigger, something that is particularly difficult to manage as, like many people with migraine, Marleen suffers from insomnia.

Not only a lack of sleep, but too much sleep, an irregular sleep pattern, or napping can result in days or weeks of intense pain for Marleen. *"For people with migraine, a small misstep – that little bit too much caffeine, that quarter of an hour late lunch – has dramatic effects, which other people find hard to grasp."*

Always very active, Marleen used to be a competitive swimmer. But when swimming began to give her awful migraines, she switched to running, which also gives her migraines but she refuses to give up on it. *"Without sports I would feel much more anxious, much more unhealthy and much more unhappy!"*

Marleen took part in the Virtual London Marathon in October 2020, raising a fantastic £1,315 for brain research. She is now training to take part in the 2021 London Marathon, and hopes to raise even more to support research into headache and other brain conditions.

"I love taking up challenges and trying new things so it was a delight and a distraction to train and fundraise for Brain Research UK last year. I am very much looking forward to the marathon this year and I hope people will continue to support this cause!"





Headache and facial pain

▼ Improving sleep in patients with chronic migraine



Dr Megan Crawford, at the University of Strathclyde, is aiming to break the cycle of insomnia in people with migraine.

Migraine is one of the most common neurological conditions, affecting around one in seven people. It is a complex and debilitating

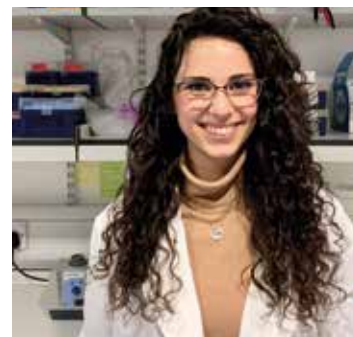
disorder with a variety of symptoms, usually featuring a severe headache.

As described by Marleen on the previous page, people with migraine often suffer from insomnia, and lack of sleep can, in turn, trigger a migraine. Treating the insomnia can break this cycle, and one of the best treatments is cognitive behaviour therapy (CBT), which teaches people to change their sleep behaviours and their thoughts about sleep loss.

CBT for insomnia (CBT-I) is currently not widely accessible, due to the limited number of trained therapists who can deliver it. Digital CBT-I, provided through an app or website, provides one possible solution. A small pilot study has shown that people liked digital CBT-I, and that it improved both their insomnia and their migraines.

As a precursor to a much larger trial, which will establish the effectiveness of digital CBT-I in reducing both insomnia and migraines, Dr Crawford is carrying out a trial run to inform decisions about design of the full study. If ultimately successful, this could enable digital CBT-I to be offered as a treatment to patients with migraine, with the potential to significantly improve their quality of life.

▼ Investigating channel and pump genes in cluster headache



Under the supervision of Professor Michael Hanna at UCL Queen Square Institute of Neurology, PhD student **Clarissa Rocca** is conducting a detailed analysis of the genetics of cluster headache, a rare headache disorder characterised by recurring

bouts of excruciating headaches.

Cluster headache has been described as one of the most painful conditions known to man, with the intensity of the pain often reported to give rise to suicidal thoughts. It impacts heavily on the lives of patients; the all-consuming pain and unpredictability of attacks can make it hard to carry on with normal life.

There are a number of treatments that aim either to stop the pain during an attack, or to stop the onset of attacks during a cluster, but they are not always effective for all patients. Unfortunately there is – at present – no cure.

Understanding the causes of cluster headache will aid the development of effective treatments, and Clarissa is building on promising preliminary data that has identified two genes that appear to be linked to the disorder. She will cast the net wider through analysis of further genetic datasets, before proceeding to study the molecular effects of these genetic mutations and how they may contribute to cluster headache. This will provide new insight into the causes of cluster headache and reveal possible new approaches to its treatment.



The Miriam Marks Fund: supporting research in neurodegeneration

Miriam Sieff was born in Manchester in 1894, and later married Simon Marks, the son of Michael Marks, business partner of Thomas Spencer. The iconic Marks and Spencer brand was born the same year as Miriam.

Miriam died with Alzheimer's disease in 1971, at the age of 77, and her family established the Miriam Marks Fund in her memory, with a £250,000 to the Brain Research Trust, one of the founding donations of this new charity.

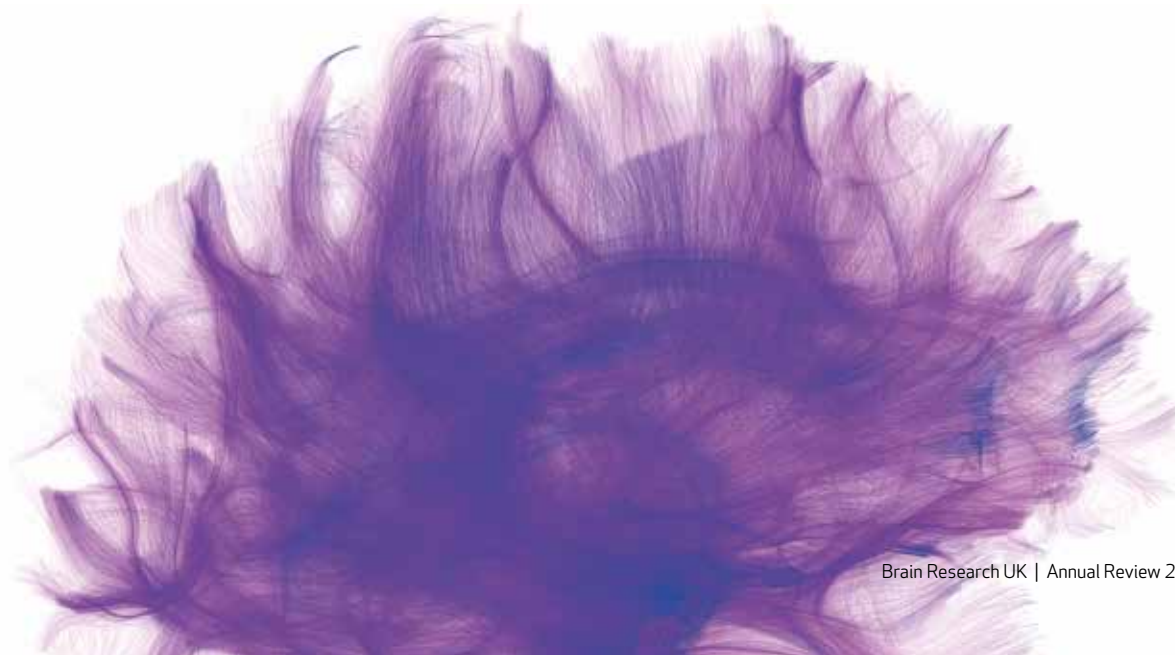
The Fund was originally intended to support research within the Institute of Neurology's Department of Neurochemistry, which was named the Miriam Marks Department of Neurochemistry in recognition of this tremendous donation.

Thanks to the generous early support of benefactors such as the Marks family, the Department thrived and expanded and is now divided into a number of different departments. The Fund has supported a range of research posts, preclinical projects and PhD students over the years since its inception, all focused on dementia and brain degeneration. The funds are now being channelled into the newly established Brain Research UK Miriam Marks Fellowship.

Brain Research UK Miriam Marks Fellowship

We have worked in partnership with UCL Queen Square Institute of Neurology to establish a new Fellowship scheme to support researchers focused on neurodegenerative diseases, funded by the Miriam Marks Fund.

We launched a call for applications in 2020 and were pleased to award the first two of these Fellowships to Professor Antonella Spinazzola and Dr Jonathan Rohrer. Their research is featured overleaf.





Brain Research UK Miriam Marks Fellowships 2020

▼ Professor Antonella Spinazzola Mitochondrial DNA dysfunction in Parkinson's disease



Professor Antonella Spinazzola is a neurologist with over 20 years' experience studying the role of mitochondria in human disease, and a Professorial Research Fellow at UCL Queen Square Institute of Neurology.

This Fellowship supports her research into the role of mitochondrial DNA metabolism in Parkinson's disease (PD), a progressive, degenerative neurological condition affecting around 145,000 people in the UK.

Mitochondria are vital components of human cells; they are the powerhouses that convert food and oxygen into energy to support cell function. When this process fails, cell deficiency and even cell death follow. While this can cause any organ to fail, the brain's high energy demand makes it especially vulnerable to mitochondrial dysfunction.

Professor Spinazzola's research has focused on the DNA molecules present in the mitochondria that produce proteins essential for energy production. Recently, her studies have led to the discovery that multiple processes and pathways impaired in PD affect, and are affected by, changes in mitochondrial DNA metabolism.

Her findings unify many earlier observations in the field of PD, and suggest that mitochondrial DNA metabolism is at the centre of a network of organelle interactions, perturbation of which can lead to PD.

With support provided by the Fellowship, Professor Spinazzola will build on these recent discoveries to further advance understanding of the role of mitochondrial DNA metabolism in brain disease and test new therapeutic approaches for PD.

PD is a debilitating condition that limits the ability of those affected to live active, independent lives. Symptoms get progressively worse and there is no treatment that can slow this decline. A treatment that could halt progression of the disease would be life-changing for those affected.

Professor Spinazzola's project aims to address this unmet need by identifying novel targets in disease-relevant pathways, and to use this knowledge to develop therapeutic inventions.

▼ Dr Jonathan Rohrer Understanding frontotemporal dementia



Dr Jonathan Rohrer is an Honorary Consultant Neurologist at the National Hospital for Neurology and Neurosurgery (NHNN) in London, and a Principal Research Fellow at Dementia Research Centre, part of the UCL Queen Square Institute of Neurology.

This Fellowship supports his research into frontotemporal dementia (FTD), the most common form of dementia in the under 60s. FTD is characterised by changes to personality and behaviour, a loss of self that contrasts with the memory problems that characterise other forms of dementia. Around a third of people with FTD have a genetic form of the disease, having inherited an abnormal gene from a parent. There are no treatments that can delay the onset of FTD or prevent its progression.

Dr Rohrer became interested in FTD as a junior doctor, intrigued by how changes to the brain can lead to the loss of self that characterises the disease. He has pursued this interest through his career, in both the clinic and the lab, determined to find out more about this disease and offer hope to those affected.

With colleagues at the NHNN, Dr Rohrer works with a cohort of around 100 families with genetic FTD. These families have been followed for many years, and he himself has been seeing them for more than 15 years.

The families offer researchers a unique opportunity to understand the earliest stages of the disease process in FTD, enabling detailed analysis of individuals known to be at high risk of developing genetic FTD but not yet symptomatic.

The team is focused on understanding the biological timeline of the disease, to establish how far in advance of the onset of symptoms there are detectable changes, and assess the implications for treatment: can treatment work when these changes have already happened, or does it need to be started much earlier, to prevent these changes?

It is only by understanding the complexities of the disease process that we can understand how to treat FTD effectively. The work being carried out by Dr Rohrer and team will help ensure that planned trials for FTD will be done in the right way: that drugs are given at the right time in order to maximise the chance of success.

There is currently no cure for FTD and the progression of the disease cannot be slowed. A number of trials are now in the pipeline and the work being carried out by Dr Rohrer and team will maximise their chance of success by enabling them to take into account the underlying biology and developmental processes of FTD.



Fundraising highlights



Virtual Virgin London Marathon and The 2.6 Challenge



◀ In June 2018, Abbie's dad Stuart collapsed at work and was rushed to hospital where he was told that he had a grade 4 brain tumour. In light of this news, so that her father could attend, Abbie and her partner booked and planned their wedding in less than six weeks. Stuart died just five days later. In April, Abbie's friend Michelle took part in the 2.6 Challenge and ran 6.2 miles with her sons on their bikes. Abbie, Michelle and another friend Sam, all nurses, will also be running the London Marathon 2021 in memory of Stuart. As part of their fundraising efforts, they have carried out bake sales, curry nights, hot chocolate stalls and have already raised an incredible £9,428.



◀ In April, Louise ran 26.2 miles locally during lockdown, supported by her sister Laura, who ran a total of 26.2 laps in her garden! They also ran the Virtual London Marathon in October, Laura in Redcar and Louise in Sheffield.

They were inspired to run by Louise's five year old son, Rufus, who has Chiari Malformation and epilepsy and together have raised an impressive £2,433.



◀ On New Year's Eve 2018, Namita sustained a traumatic brain injury at her local gym that led to post-concussion syndrome and chronic migraine for over a year. The London Marathon 2019 was her first public outing after the injury and it inspired her to enter the ballot for the 2020 marathon, where she successfully gained her Own Place. In choosing to run for the charity, she wanted to help raise awareness of brain conditions. She successfully completed the Virtual London Marathon in October 2020 and raised a wonderful £8,697.



◀ Roger, a supporter for over 15 years, lost his wife and several family members to the vagaries of brain conditions. He ran the Virtual London Marathon in Chester dressed as Axl Rose, from his late wife's favourite band. He has also run the full length of the Liverpool to Leeds canal, 130 miles non-stop, and seven marathons on seven continents in seven days. Thanks to his hard work and incredible effort over the years, Roger has raised a staggering £29,000.



◀ In September 2017, Nick's wife Adele suffered two strokes that resulted in several health complications and multiple weeks spent in hospital. Nick ran the Virtual London Marathon and raised an excellent £3,564.

● Alzheimer's disease has affected Tom and his family personally; his friend lost her fiancé to a brain tumour and his partner Nicola was diagnosed with a benign brain tumour. In October, Tom braved the wind and rain and completed a 26.2 mile run from his home and raised a superb £1,328.



◀ Debbie and Richard were joined by their family in April to run 2.6 miles for the 2.6 Challenge. Richard was dressed as a brain and Debbie as a scientist to help raise funds, awareness and a smile from all those around them. They both also completed the Virtual London Marathon in October. They chose to run for us as Debbie's close friend suffered from a brain abscess, her grandmother had dementia and Richard's grandmother suffered with a stroke. Together, they raised a terrific £2,821.



◀ In October, Angie took on the Virtual London Marathon with the support of her friends and family and raised a brilliant £3,005. Angie is also running the London Marathon 2021 for her mum, who suffered a life-changing stroke in 2014.





Other virtual runs and challenges



◀ In September, Sammy took on the Virtual Great North Run with her fiancée, Claire. She supports the charity as a result of her personal experiences with a brain cyst, hydrocephalus and migraines. Running 13.1 miles from their doorstep, Sammy and Claire raised a fantastic £751. *"I have a brain cyst that caused hydrocephalus*

and have had a fair few surgeries to get a VP shunt sorted. Before finding out the cause, I had quite debilitating migraines so know first hand the impact neurological conditions can have on a person's life. Thank you for all that the charity does!"

● In January, Tom and Ellie each ran 50 miles in memory of their friend, Lewis, who passed away from a brain bleed at the age of 21. Tom met Lewis when he was young and always looked up to Lewis who was both kind and genuine. They raised a stunning £3,010 from their challenge. *"Fifty miles was a challenge for me, although I'm sure it was a breeze for my friend Ellie who runs competitively. Keeping to a schedule certainly kept my physical and mental fitness on track during lockdown. We undertook the challenge as a tribute to our dear friend Lewis and his family and to help raise awareness and funds for Brain Research UK."*

▼ Bethany was completing the second year of her MBIol Neuroscience degree at the University of Leeds when she decided to organise her own challenge: to cycle 90 miles (representing the fact that someone is admitted to hospital with a brain injury every 90 seconds) over 6 days (representing that 1 in 6 people suffer from a neurological disorder). Starting on 3rd August, Bethany successfully completed her challenge on 8th August raising a fabulous £232.



◀ In July, Dom ran a mile every hour for 24 hours, starting off at 4am and finishing the following day at 3am. He managed to raise an admirable £213 in memory of the mother of his childhood friends Tasha and Olly, who sadly passed away from Sporadic Creutzfeldt-Jakob disease in 2016. Although extremely physically and mentally challenging, he received a great deal of support from family and friends and found the challenge hugely rewarding.

● In 2015, Magda suffered from a brain haemorrhage and was subsequently diagnosed with an arteriovenous malformation on her brain stem. As a survivor of a brain injury, which resulted in her needing to use a wheelchair, Magda took on a challenge to cycle 12 km a day for 24 days during February using her recumbent exercise bike, raising an excellent £670. *"I decided to support Brain Research UK because I am a brain injury survivor myself and totally understand the importance and magnitude of their work!"*

▶ In November, Jasmeen, her brother Sahib and her two cousins Aman and Karam took part in a sponsored cycle in memory of their grandmother, Tarsem, who passed away from a brain haemorrhage earlier in the year.



To commemorate their grandmother's 88th birthday, they each cycled 50 km from their doorsteps and raised a tremendous £1,179. *"Our grandmother Tarsem, also known as our Bibi Ji, was a kind, loving person who dedicated her life to her family and to her religion. She was the strongest person in our lives, beating cancer, TB, and even had to suffer the loss of her first child. No matter what came in her way, our grandmother always had a smile on her face and, along with my grandfather, she did everything she could to give us a future. We wanted to do this charity bike ride in memory of her, as a key teaching of our religion is 'Vand Chhako', which teaches us to share what we have with others who need it the most. As challenging as the bike ride was, we pushed through as we knew she would be so proud of us. We will continue to raise money in her memory."*





Community fundraising

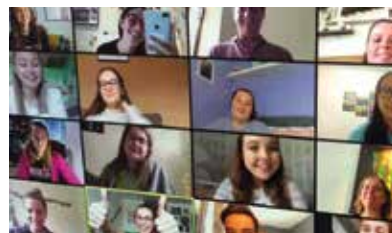


◀ At the age of 6, James was diagnosed with a golf ball sized brain tumour, a ganglioglioma, which caused him to develop uncontrollable epileptic seizures.

These, together with the strong medication he received, affected his memory and personality. He experienced many difficulties and missed years of full-time education. In 2017, after nine hours of surgery, most of the tumour was removed. Now, aged 12, James is living the normal life of a teenager, only on a low dose epilepsy medication. In 2020, his mum Jane started selling bespoke handmade personalised gifts to raise money for brain research and, over the last year, has raised a remarkable £2,000. *"If it weren't for the work of charities like Brain Research UK, many of our loved ones would not be alive today. The more funding they get, the more lives will be saved in the future. I feel what I do is a drop in the ocean – but just look at the ripple that comes from one drop."* A big thank you also to James who kindly drew the image for our 2020 Christmas card.



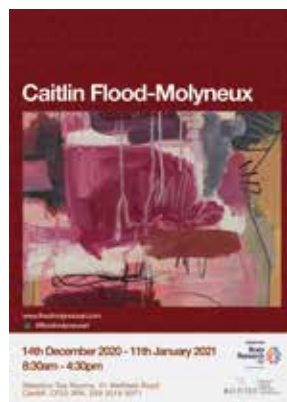
◀ In February, Alex and Martha's challenge was to walk 15 km a day for 15 days. They are both Psychology students at the University of Southampton who, after studying brain diseases, decided to support the charity to help the advancement of research in cognitive areas such as memory. They raised an inspiring £229.



◀ In August, the cast of Waitress UK, including our London Marathon runner Sarah, took part in a virtual Q&A session organised by fan, Nicole. This event

was a great success, giving fans the chance to meet their favourite characters, and raised a fantastic £250.

● Kira, aged 7, earned her Charity Badge from her local Brownies club in December by learning and talking about our charity with her fellow Brownies, and by selling stickers and hand-drawn pictures to friends and family. She raised an impressive £35 to help people like her mum, Helen, who has had brain surgery.



◀ Caitlin held an art exhibition in Cardiff in December in memory of her mum, Julie, who passed away from a sudden brain haemorrhage and who greatly inspired Caitlin and encouraged her to travel and to pursue her passion in art. She raised a splendid £385.



We are enormously grateful to the following long-term supporters who were determined to go ahead with their planned annual events, turning them virtual this year!



▲ Tasha holds an annual walk in memory of her mother Mandy, who died from Sporadic Creutzfeldt-Jakob disease (CJD). Not wanting to cancel the event, she asked friends and family to undertake a virtual memory walk on the day and succeeded in raising a wonderful £1,016.



◀ In October, Julie successfully completed the Virtual London Marathon with the support of family members who cheered her across the finish line. She ran for her sister Ann, who had a tumour behind her ear, and for her nephew who has epilepsy. Ann supported her sister's fundraising by holding her annual Christmas lights display two years in a row. Together, the sisters have raised a staggering £5,013.

● For a number of years, Chelsea Flower Show award winner Anthony holds plant sales at his home in memory of his father who had motor neurone disease. This year, he decided to email a list of plants and prices to his contacts, taking payments online and arranging for people to collect their plants on a specific day and time from his front doorstep! The sale raised a fabulous £3,035.

● Sally and David raise funds in memory of Sally's father who died as a result of a glioblastoma. Instead of holding the event in their beautiful barn as usual, they organised not just one but two virtual piano recitals during the year raising a tremendous £5,227.



Thank you

A sincere and heartfelt thank you to each and every one of the thousands of people who have so kindly supported us, physically and virtually, during this difficult year.

Whether you generously donated or gave a gift, ran a marathon, took part in an event, volunteered your time, shared your story or undertook one of the other numerous and creative activities as a result of Covid-19... for all that you have done, thank you.

It is only thanks to your valued support that we are able to fund vital research to help those with a neurological condition live better, longer.

With special thanks to the following for their valued support:

- Dr Faisal Amin
- Professor Rob Brownstone
- Robin and Jim Buchanan
- Bryan Guinness Charitable Trust
- Busy Bees Nursery
- CBRE
- Professor Alasdair Coles
- Collier Capital
- Constance Travis Trust
- Mrs E C Davies
- Dora Rebecca Fine Charitable Trust
- Florian Charitable Trust
- Professor Oliver Hanemann
- Professor Henry Houlden
- Innospec Limited
- Simon Irons
- Lyondellbasell NV
- Jane and James Millar
- Our peer reviewers
- Professor Simona Parrinello
- The Thomas Sivewright Catto Charitable Trust
- Tim Rogers
- Professor Alexandra Sinclair
- Professor Kevin Talbot
- Professor Nick Ward

We thank Sherbrooke Connectivity Imaging Lab (<http://scil.dinf.usherbrooke.ca>) M. Chamberland and M. Descoteaux and Science Photo Lab (www.sciencephoto.com) for images used in this report.



Our performance



Our ability to fundraise during the year was significantly constrained by the Covid-19 pandemic, especially with the cancellation of the London Marathon in 2020. As a result of the pandemic, our events and community fundraising activities for the year changed into virtual activities and, as much as possible, we maintained other fundraising activities in order to fulfil our aims and objectives.

With the marathon being our flagship fundraising event, and the difficulty of being able to undertake other forms of community or event based fundraising, our events income fell to £181,000. The fall in income has been partially offset by fundraising from trusts, corporates and major donors amounting to £231,000 and an increase in the number of legacies received this year amounting to £557,000.

The change in operating model that was implemented in previous years meant that our operations remained lean and adaptable to change. Consequently, we were able to reduce our expenditure on raising funds to £722,000. In addition, we were able to utilise some savings in our overheads without having to obtain government assistance through any emergency Covid-19 scheme.

Despite the challenges, we were pleased to be able to increase the amount spent on our charitable activities to £2,589,000, compared to previous financial year. This included direct research spend of £2,355,000.

This means that for every pound we spent during 2020/21, **78 pence** was spent on our charitable activities – an increase on the previous 18 months (67 pence).

We ended the year with an operating deficit of £1,560,000 but, after benefiting from significant investment gains of £2,249,000, increased our funds reserve position by £689,000. At 31st March 2021, our total reserve position was £11,574,000.

Our objectives for 2021/22:

As a result of on-going uncertainty around Covid-19, our objectives for 2021/22 are as follows:

Our objectives for research activities:

- To sustain our core funding of two national calls for PhD studentships and project grant funding
- To deliver a meaningful Impact Report to reflect our 50 year anniversary in October 2021

Our objectives for fundraising activities:

- To develop further our unique, as well as collaborative, event and challenge activities
- To develop further our major donor fundraising activities

The Trustees understand that the benefits of neurological research is long-term but believe that the knowledge gained from each research project funded is a step towards understanding how these diseases happen and how to treat them. Trustees also understand that measuring the impact of their donations is an important consideration for those who give so generously to support the Charity's work.

Our finances



The previous period reflects 18 months of activity from 1st October 2018 to 31st March 2020.
The current period reflects a 12-month financial period from 1st April 2020 to 31st March 2021.

	2021 12 months £'000	2020 18 months £'000
Our income		
Individuals	414	689
Trusts, corporates and major donors	231	174
Income from events	181	853
Legacies	557	104
Total donations income	1,383	1,820
Investment income	368	681
Total donations and investment income	1,751	2,501
Our expenditure		
Raising funds	722	1,207
Charitable activities	2,589	2,462
Total expenditure	3,311	3,669

This summarised financial statement has been extracted from the full trustees' annual report and financial statement as approved by the trustees on 25th June 2021. The full financial statements, which our auditors haysmcintyre have given an unqualified audit report, will be submitted to the Charity Commission and to the Registrar of Companies.

The auditors have confirmed that, in their opinion, this summarised statement is consistent with the full statement for the year ended 31st March 2021.

The full trustees' annual report and financial statement and auditors' report may be obtained from Brain Research UK, BWB Charity Hub, 10 Queen Street Place, London EC4R 1BE or brainresearchuk.org.uk


Together we can accelerate the progress of brain research.
Please support us by donating, volunteering or fundraising.



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Registered in England No. 7345516.

