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1 Introduction

Established in 1971, the original remit of the Brain Research Trust was to raise funds to support research at the Institute of Neurology, University College London. The new charity achieved remarkable early success in attracting some major donations that galvanised research into neurological conditions, helping to lay the foundations for a wealth of research that has taken place at the Institute over the last 50 years, and driving progress in our understanding of neurological disease.

In 2015, we broadened our objectives to enable us to fund nationally, and our name was changed to Brain Research UK. A review of research strategy considered the case for focusing our research funding on a limited number of specific disease areas. Taking into account the level of unmet need and the levels of existing funding, we elected to prioritise the following three disease areas:

- **Neuro-oncology**
- **Acquired brain and spinal cord injury**
- **Headache and facial pain**

We subsequently launched a national call for applications for PhD studentships, followed by a call for project grant applications, both focused on these priority areas. These schemes have run annually since 2016. We have received and assessed a total of 614 funding applications, leading to the award of 43 grants, worth £9.9 million (as at December 2023).

As well as directly addressing important research questions in the three priority areas, a key aim has been to build capacity in these fields of research, to help increase momentum and facilitate continued progress. This is being achieved not only through the PhD studentships, through which we have aimed to provide early support for talented young researchers, to wed them to these research areas, but also through the project grants, through which we have specifically encouraged applications from early career researchers.

Our relationship with the Institute of Neurology remains strong. We continue to fund research there through our competitive national calls as well as through some restricted endowment funds that we still hold. We have also worked in partnership with the Royal College of Surgeons of England to co-fund four neuro-surgical fellowships.

A review of our research strategy this year is timely in order to reflect upon the grants that have been awarded, identify any changes in the landscape, and evaluate opportunities to improve our grant-making and increase the impact of our funding towards benefit for those affected by neurological conditions.

2 Our research aims

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

Working towards this vision, we are focused on two aims:

- To fund high quality research in areas of unmet need that will advance understanding of neurological conditions, to advance diagnosis and treatment, and deliver translational impact within a five- to ten- year timeframe.
- To nurture the next generation of neurological researchers in order to increase research capacity and build the critical mass that is necessary to drive progress in areas of unmet need.

3 Priority research areas

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

Since broadening our objectives to fund nationally in 2015, our funding schemes have focused on three priority areas: **neuro-oncology**, **acquired brain and spinal cord injury**, and **headache and facial pain**.

Focusing our funding in this way enables us to achieve a greater impact than would be possible if we spread our funding across the full range of neurological conditions. These three themes were selected on the basis that they were areas of significant unmet patient need, without substantial dedicated research funding.

There has been a welcome increase in the level of funding devoted to brain tumour research since 2016 (see section 6), partly due to the influence of the late Dame Tessa Jowell, but it remains an area of high unmet need. In brain injury, funding was announced in 2023 for a new research platform to coordinate research in traumatic brain injury (TBI), an important development that promises to accelerate progress in this area of continued high unmet need (see section 7). There has been no change to either the funding landscape or the level of need in headache and facial pain. All three research areas remain areas of high unmet need and we plan to continue funding in these priority areas, to build on progress made.

The remit of each the three themes is set out in *figure 1* below. This wording is regularly revisited, in light of applications received under each call, to ensure that it clearly conveys our aims. We introduced the development of disease models as a complementary theme in our 2023 project grant call, and this will be maintained.

Figure 1: funding remit

We will accept applications for the funding of hypothesis-driven pre-clinical or clinical research that addresses areas of large unmet need and demonstrates a clear pathway to clinical impact in one of our three priority areas, below. *Projects must have a mechanistic hypothesis and a clear pathway to translation.*

Additionally, we will fund the development of models that enhance these three themes and facilitate translation. *Models may be in vivo or other 3D models, and must support the future testing of a mechanistic hypothesis.*

Priority themes

1. Neuro-oncology

We want to fund research that aims to improve clinical outcomes for patients with primary tumours of the brain or spinal cord. We will fund research that addresses the fundamental causes, mechanisms, diagnosis or treatment of primary tumours of the brain or spinal cord, and associated neurological complications.

2. Acquired brain and spinal cord injury

We want to fund research that aims to protect or restore function in patients with acquired brain or spinal cord injuries. We will fund research that addresses the mechanisms of the injury, the mechanisms of the recovery process, and determinants of outcome.

3. Headache and facial pain

We want to fund research that aims to improve the management and treatment of headache or facial pain disorders. We will fund research that addresses the fundamental causes, mechanisms, diagnosis or treatment of headache and facial pain.

Figure 2, below, shows how funds awarded to date have been distributed across the three priority areas. This distribution of funds should be considered in light of the volume of applications received under each theme. We receive a lower volume of applications in Headache and facial pain than in the other two themes, as shown in figures 3 and 4. This in itself is reflective of the paucity of research taking place in headache and underscores the importance of this theme.

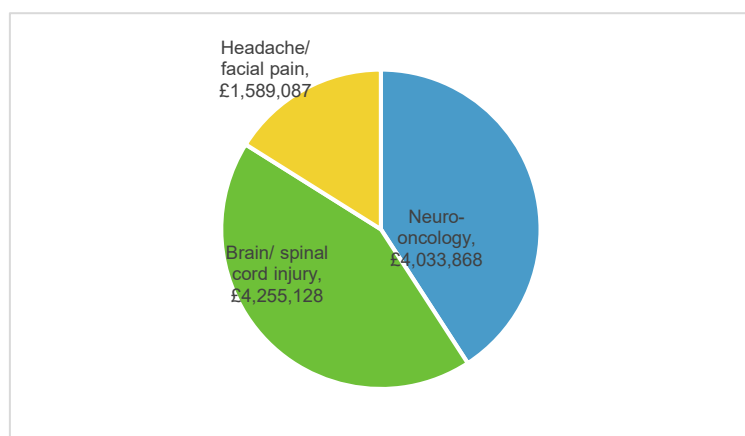


Figure 2

Breakdown of awards granted by disease area, 2017 to 2023

(43 grants, total value £9.9 million)

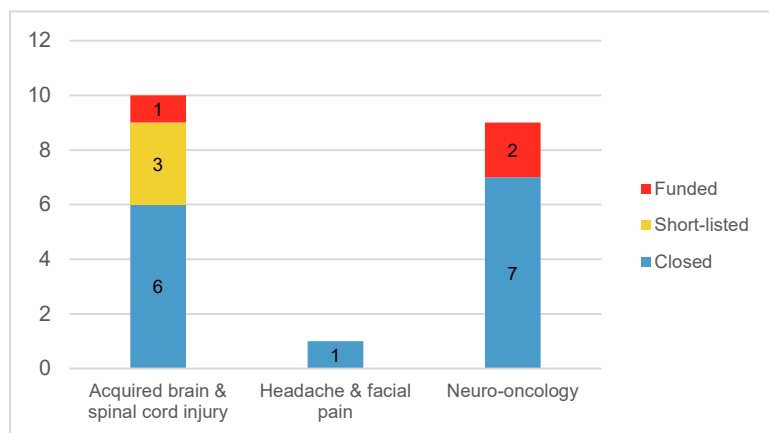


Figure 3

2022/23 PhD studentship call – applications received

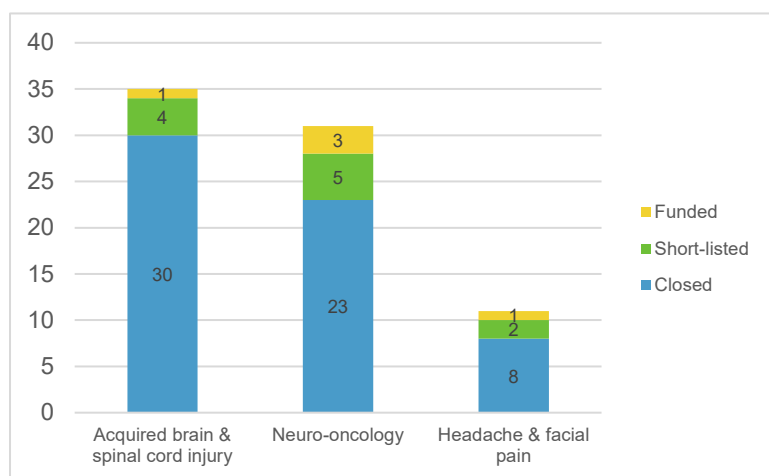


Figure 4

2023 project grant call – applications received

When allocating funding, our driving principles are scientific excellence and translational impact. Whilst we like to achieve a balance across the three priority areas, we do not have quotas for each priority area.

To try to address the imbalance in funding, in respect of the amount of funding devoted to Headache and facial pain, we will increase efforts to disseminate our calls to relevant groups. We will also improve the feedback given to unsuccessful applicants (across all three themes) so as not to discourage future applications from individuals or groups who are unsuccessful with an application in one call. The introduction of the models theme should also benefit those working in headache, as the lack of valid disease models has been highlighted as a particular issue in headache research.

Each of the three priority areas is discussed in further detail in sections 6, 7 and 8 below.

Priority research areas: Summary

- We will continue to fund research in the same three priority areas: neuro-oncology, acquired brain and spinal cord injury, and headache and facial pain.
- We will maintain the complementary disease models theme.
- We recognise that there is an imbalance in the level of funds awarded under the three priority themes; this is a reflection of the low number of applications submitted under the headache theme. We will increase efforts to disseminate our calls to relevant groups, and we will also take steps to improve the feedback given to unsuccessful applicants.

4 Funding schemes

There are three aspects to our current grant-making – our national, competitive funding schemes, our endowment funding, and our partnership funding.

4.1 National funding schemes

Since 2016 we have run annual calls for project grant and PhD studentship applications focused on our three priority research areas.

Project grants

Our project grants provide funds of up to £300k for projects lasting up to three years. Since 2016 we have received and assessed 428 project grant applications, resulting in the award of 27 project grants (as at December 2023).

Since 2020 we have specifically encouraged applications from early career researchers (ECRs), to support the aim of growing capacity in our priority research areas. We have subsequently awarded funding to six ECRs.

The project grant scheme is popular and highly competitive, with 77 applications submitted in 2023, and has enabled us to fund high-quality research across our priority areas.

We therefore plan to maintain this scheme, with the maximum grant size remaining at £300k. We expect to make four awards annually.

PhD studentships

Through our PhD studentships, we have offered funding of up to £130k to support PhD students for up to four years. The aim is to support promising researchers who we hope will go on to develop careers in the under-resourced fields on which we are focusing our funding. Since 2016 we have received and assessed 186 studentship applications, resulting in the award of 17 studentships.

Our preference to make personal awards, rather than supervisor-led awards, has been a central tenet of this scheme and we have funded outstanding individuals, who have delivered exciting and impactful research projects in our priority areas.

The extent to which we are achieving our aim of building capacity in the priority research areas is unclear, however. The studentships provide short-term funding to individuals at a career stage when it is early to make long-term decisions about future focus and it not clear that these individuals will stay in their respective fields.

We believe that we can more effectively fulfil our aim of building capacity in the three priority areas by repurposing the funds to support post-doctoral fellowships. Accordingly, we do not propose to run further calls for PhD studentship applications. We will, however, continue to fund clinical PhD studentships as part of the new post-doctoral scheme, below.

Post-doctoral fellowships

There is a recognised bottle-neck in funding for post-doctoral researchers looking to establish independence. In 2024 we will launch a new post-doctoral fellowship scheme to help address this.

We believe that this will help us to achieve our aim of building capacity in our three priority areas; injecting funds at this important career stage will aid career development, and aid retention in the field. In recognition of the shortage of research-trained clinicians, the scheme will also be open to prospective clinical academic PhD students.

Post-doctoral fellowship scheme overview:

- The scheme will be open to applicants who have a PhD in a relevant discipline, or who have a medical degree and wish to undertake a PhD.
- There will be no upper or lower limit on the number of years' post-doctoral experience but those who already have their own lab, or who hold, or have held, an equivalent competitive fellowship will not be eligible to apply.
- We will provide funding of up to £300k for three years full-time, or part-time equivalent.
- The first call will be launched in Spring 2024.

4.2 Endowment funding

We continue to hold three endowment funds, each established in the early days of the charity, each containing funds restricted to UCL Institute of Neurology (IoN) and, within that, restricted to research in specific disease areas. It has been agreed by our Board that all three funds are expendable, and the expectation is that each will be spent down in the next five to ten years.

The **Sobell Endowment** was created in 1975, with a £250,000 gift from Sir Michael Sobell. The intention was to establish a Chair of Neurophysiology at the IoN. This Chairship was taken up by Professor Tom Sears in 1975, and subsequently funded his successor, Professor Roger Lemon until he retired in 2012. The endowment funding enabled basic research in multiple sclerosis, motor neurone disease and spinal cord trauma, and the Sobell Department of Neurophysiology gained national and international recognition for its research.

After some years funding core costs in the department, funding for the Chairship was re-established in 2022, with the award of funds to support Professor Linda Greensmith, Head of the Department of Neuromuscular Diseases (which encompasses the Department originally known as the Department of Neurophysiology). It is expected that the endowment will be extinguished with a renewal of this funding in 2025.

The **Marks Endowment** was established in 1973 with a £250,000 donation from the Miriam Marks Charitable Trust in memory of Mrs Miriam Marks, who had suffered from Alzheimer's disease. The funds were to be applied to '*research work on dementia and brain degeneration within the Department of Neurochemistry*'. The early application of these funds is not recorded but more recently funds were used to support PhD students at the IoN working on projects related to dementia and neurodegeneration.

In 2020, we worked with the IoN to call for applications for Brain Research UK Miriam Marks Senior Research Fellowships. Two awards were made, each supporting a Research Fellow for two years, including salary and research costs. In 2023, following discussion with the IoN, the Fellowships were refocused to support junior post-docs and two further Fellowships were awarded, this time for three years each. There are sufficient funds to support several further cycles of fellowships and a timetable will be established with the IoN.

The **Watts Fund** was established with a gift of £855k from the Will of Miss Eileen Watts in 1994 in memory of her brother Graeme, who had motor neurone disease, and was later supplemented with a further legacy. These Funds were initially to be used to support an academic appointment in Graeme's name at the IoN for research into MND, and thereafter at the Trustees' discretion.

Linda Greensmith was recruited to the post of Graeme Watts Senior Research Fellow in 1999, with Watts Funding also supporting a research technician and refurbishment of laboratory space. The salary of Linda Greensmith was taken on by the IoN after ten years, but we continue to fund the laboratory manager, with funding renewed most recently in 2018. A five-year programme grant was awarded in 2019. The funds are likely to be extinguished within five to ten years, following renewal of the lab tech funding and a potential new programme grant.

4.3 Collaborative working

We will build on existing collaborations and look for new opportunities to work collaboratively with other organisations to further research in our three priority areas, to complement our own funding initiatives.

We will seek to establish collaborations that do not divert funding from our own initiatives but rather add value to these by, for example, working with funders whose aims synergise with our own and can add value by broadening our reach, increasing the funds available, or improving efficiencies.

Funding schemes: Summary

- We will continue to run annual national calls for project grant applications.
- Our PhD studentship scheme will be replaced with a new scheme offering post-doctoral fellowships. This new scheme will also be open to prospective clinical PhD students.
- We will continue to steward our three endowment funds to support relevant research at UCL Queen Square Institute of Neurology.
- We will look for opportunities to work collaboratively with other organisations to further research in our three priority areas, complementing our own funding initiatives.

5 Funding processes

Our aim is to fund research that has the best chance of delivering meaningful impact for those affected by the conditions on which we are currently focused. To ensure that we succeed in funding the best research, our application and assessment processes must be straightforward, robust and transparent.

Since the launch of our project grant and studentship schemes in 2016, we have received and assessed 614 funding applications. These represent countless hours of work – on the part of the applicants, the members of our Scientific Advisory Panel (SAP), external reviewers and staff. To avoid wasted effort, we have a responsibility to all involved to:

i. Be clear and specific about the remit

The wording of our calls is kept under review. After the conclusion of each call, members of the SAP reflect on the applications received and discuss whether any changes are needed to improve clarity in terms of the types of applications being sought.

ii. Ensure that our application processes are straightforward

We recognise the burden on researchers of the constant cycle of funding applications and deadlines, and we appreciate the effort and time required to submit applications of high quality.

We strive to make our application processes as user-friendly as possible. Our two-stage application process for the project grants helps to minimise wasted effort; the preliminary stage involves submission of a short project overview and only those short-listed through to the second stage are required to submit a detailed research proposal. At this stage there is usually a success rate of at least one in four, with 12 to 16 applications short-listed for three to four grants.

We implemented an online application system in 2021 and continue to refine and improve the way we use this, to streamline the process for all involved.

iii. Ensure that our assessment processes are robust and transparent

Our competitive funding schemes have an assessment process that involves initial triage by the members of our SAP before external review of short-listed applications. Our assessment processes are set out in the call documents.

All short-listed applications go out for external peer review before returning to the SAP for further discussion. Funding decisions do not rest entirely upon the scores and opinions of the external reviewers, but also take into account differences of opinion between reviewers, differences in the number of reviews obtained, and differences in the level of scrutiny applied by reviewers. Panel members must form a view as to where the applications sit relative to each other.

We will continue to strive to obtain a range of high-quality reviews for each short-listed proposal, ensuring that a sufficient window of time is built into the timetable. A revision to the timelines for the two funding streams, which aims to avoid applications going out for review over the summer holiday period will facilitate this.

We have a clear process for the management of conflicts and by maintaining a panel that is broad in focus, with experts from the different priority areas, we strive to avoid bias.

Individualised feedback is now given at both application stages. Going forward, the second stage feedback will be discussed and agreed during the panel meeting; this will improve the quality of the feedback and also help ensure robustness of decision-making.

We will publish data on success rates.

iv. Equality, diversity and inclusion

We are committed to achieving equality of opportunity for all funding applicants. Applications are assessed on scientific merit, and the track record (and future potential) of research applicants. We support a diverse range of researchers from Institutes around the UK.

We do not currently collect data on EDI and will review whether this should be implemented.

v. Patient and public involvement

We do not currently incorporate patient and public involvement (PPI) in our funding processes, but recognise the importance of doing so. We will consider ways of meaningfully incorporating PPI, and will also review how we ask applicants to incorporate PPI.

Funding processes: Summary

We will continue to strive to make our application and assessment processes as open and straightforward as possible. In particular we will:

- Be clear and specific about the remit
- Ensure that our application processes are straightforward
- Ensure that our assessment processes are robust and transparent
- Review whether we should collect EDI data
- Consider how to incorporate PPI into our research processes.

6 Priority area 1: Neuro-oncology

Brain and spinal cord (CNS) tumours were highlighted as a research priority in 2016 because of the high level of patient need, combined with low levels of historic and current research funding. CNS tumours remain an area of significant unmet need, responsible for significant mortality and morbidity.

We call for applications meeting the following remit:

Neuro-oncology

We want to fund research that aims to improve clinical outcomes for patients with primary tumours of the brain or spinal cord.

We will fund research that addresses the fundamental causes, mechanisms, diagnosis or treatment of primary tumours of the brain or spinal cord, and associated neurological complications.

We will also fund the development of models that enhance this theme and facilitate translation. Models may be in vivo or other 3D models, and must support the future testing of a mechanistic hypothesis.

6.1 About CNS tumours: the facts

- Around 12,300 people are diagnosed with a new primary CNS tumour every year in the UK¹.
- These tumours are responsible for around 5,500 deaths annually in the UK, including more deaths in people under 40 than any other cancer².
- Only 41% of adults diagnosed with a brain tumour in the UK survive one year from diagnosis. Just 12.5% survive five years³.
- Children have a better prognosis, with 77% of children (aged 0 to 14 years) surviving five years from diagnosis⁴, but this can come at substantial cost, with the treatments used commonly giving rise to substantial cognitive disability and other health problems.

The relatively high overall survival rates in children mask some grim statistics, however, with some tumour types having an exceptionally poor prognosis in the face of a lack of effective treatments. The high-grade brain stem glioma *diffuse intrinsic pontine glioma* (DIPG) is incurable with current treatments. Median survival for young patients (aged 0 to 19 years) with high-grade brain stem gliomas, most of which are DIPG, is just 15 months⁵.

Other tumour types – including ependymoma and medulloblastoma – have been highlighted for the lack of improvement in survival. A 2021 report by the National Cancer Registration and Analysis Service (NCRAS) reported five-year survival of 73% and 69% respectively for these two tumour types in children diagnosed in the UK between 2012 and 2016⁴.

The NCRAS attributes the gradual improvements in survival for childhood CNS tumours to a range of factors, including specialisation of diagnostic imaging, molecular pathology and histopathology, and technical refinements in neurosurgery and radiotherapy. The report notes a survival link to clinical trials, underlining the desperate need for more clinical trials for all brain tumour patients.

One explanation for the lack of progress for patients with high grade brain stem gliomas is the paucity of available tissue for research. The risk of biopsy has historically been considered too great, meaning that diagnosis has been largely achieved via imaging, limiting biological insights and ability to carry out molecular and genetic profiling to identify new treatment targets. This is changing, with biopsy and molecular profiling now central to

diagnosis, and this will positively impact research and pave the way for the use of targeted treatments in these young patients.

6.2 Review of Brain Research UK neuro-oncology funding

As outlined in section 2, our national calls attract a substantial volume of applications under the neuro-oncology theme, and it is well-represented amongst the applications that are short-listed and subsequently funded.

Since 2017 we have funded 18 brain tumour projects (11 project grants and 7 PhD studentships), worth a total of £3.1m.

Figure 5 below shows the breakdown of awards by tumour type. The high proportion of glioblastoma (GBM) projects funded reflects the high number of applications typically received.

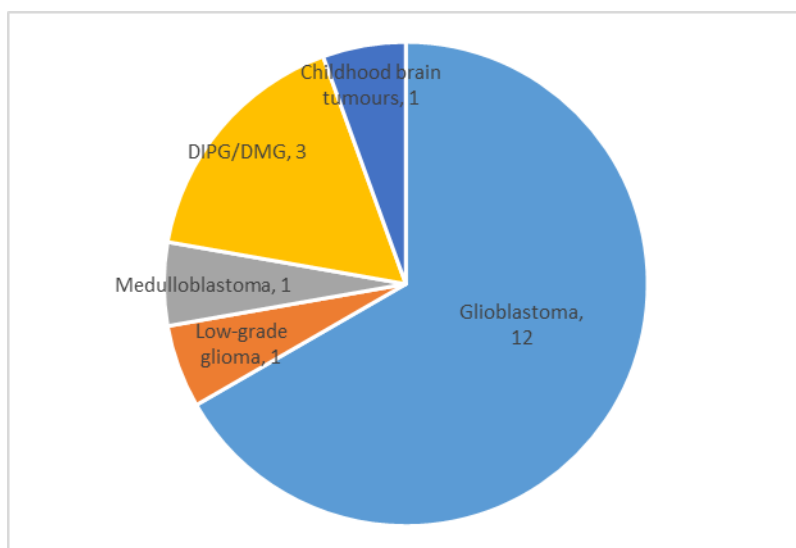


Figure 5

Brain tumour grants awarded, 2017 to 2023, by tumour type

6.3 External funding landscape

There has been increased attention given brain tumours in recent years, thanks in part to the work of the late Dame Tessa Jowell and the 'Brain Tumour Mission' established in her name. Funding by partner charities of the National Cancer Research Institute (NCRI) increased from £8m in 2015/16 to £17.6m in 2020/21 (£17.6m)⁶ - an increase from 3.3% to 5.5% of site-specific cancer research funding.

Despite this increase, however, the £18m investment in brain tumour research in 2020/21 still pales in comparison with the amount devoted to cancers such as breast (£52m, 76% 10y survival, up from 40% in 1971; 60k annual cases), bowel (£40m, 53% 10y survival, up from 22% in 1971; 43k annual cases), and leukaemia (£34m, 46% 10y survival, up from 6% in 1971; 10k annual cases). The dramatic improvement in survival rates for these better-funded cancers shows what can be achieved with more substantial funding.

Increased, sustained funding is required if we are to build on recent progress in research and translate this to improvements in clinical outcome for patients with brain tumours.

The three leading charitable funders of brain tumour research in the UK are Cancer Research UK, the Brain Tumour Charity, and Brain Tumour Research.

Cancer Research UK spent just under £12m on brain tumour research in 2021/22, with £28m committed to '*strategic initiatives in brain tumour research*' over five years from 2018 – including ring-fenced funding calls, capacity-building centres of excellence and a radiation research network with a major focus on brain tumours.

The Brain Tumour Charity had a research spend of £5m in 2022. They have two current funding streams. 'Quest for Cures: Collaborative Discovery Teams' offers up to £1.5m per programme over five years to support 'collaborative discovery teams with transformational research ideas'. 'Future leaders' provides up to £225k initially, for three years, or potentially £1.8m over 12 years to fund 'the future leaders of scientific and clinical research into brain tumours'.

Brain Tumour Research had a research spend of £1.5m in 2021. They provide core funding to support Centres of Excellence around the UK to build the critical mass of expertise needed to accelerate progress. Current centres are the Institute of Cancer Research, University of Plymouth, Queen Mary University of London, Imperial College London and University of Portsmouth.

6.4 External reports on neuro-oncology research

The **NCRI Brain Group** is 'a multi-disciplinary community of researchers and consumers focused on clinical and translational issues relating to brain tumour research'. The group works with clinical research networks, funders and national and international researchers to develop research to improve outcomes for brain tumour patients and identify areas of unmet need. The group identified their strategic priorities in 2021 to address challenges faced in brain tumour research and to ultimately improve outcomes for brain tumour patients⁷. These included: publication of a paper on the challenges in brain tumour research, and proposed solutions; developing a window of opportunity study, early-phase trial or basket study for glioblastoma patients utilising targeted agents, immunotherapy and/or drug-radiotherapy combinations; developing an innovative research trial to improve outcomes for brain tumour patients with unmet needs; improving outcomes for elderly or frail patients, patients with poor prognosis and patients ineligible for active oncological treatment; building and strengthening links with international groups and prioritizing opening international studies for UK patients with rarer brain tumours; supporting and providing guidance for a broad range of research proposals across the brain cancer community via regular proposal guidance meetings. Unfortunately the NCRI closed in 2023 and, at the time of writing, the future of the Brain Group is unclear.

The **James Lind Alliance** published a **Priority Setting Partnership in Neuro-oncology** in 2015⁸. This collaboration between CNS tumour patients, carers, major brain and spinal cord tumour charities and multidisciplinary professional organisations generated a 'top ten' of research questions that are important to patients and carers. It is important to acknowledge these patient priorities, especially in light of the fact that we don't currently have any patient representation on our assessment panels, however many of the questions identified are outside the scope of our research funding – including questions that are qualitative, epidemiological or social in nature without addressing mechanistic aspects of the disease.

Questions that are potentially of relevance are listed below, **bearing in mind our requirement for a mechanistic hypothesis**. Most of these questions would require the inclusion of a mechanistic question to be in remit:

Those with an asterisk are included in the top 10, others are questions that were discussed at the workshop, but not in any order of priority.

- Do lifestyle factors (e.g. sleep, stress, diet) influence tumour growth in people with a brain or spinal cord tumour?*
- Do molecular subtyping techniques improve treatment selection, prediction and prognostication in people with a brain or spinal cord tumour?*
- What are the long-term physical and cognitive effects of surgery and/or radiotherapy when treating people with a brain or spinal cord tumour?*
- In brain tumour patients, what is the effect of cognitive interventions (including memory training) on improving memory after radiotherapy, compared with standard care?
- Does chromosomal analysis of low grade gliomas improve prediction of transformation to a higher grade?

- In malignant brain tumour patients, how effective are complementary and alternative medicines, which include supplements and herbal remedies, compared to standard treatment alone, for extending and improving quality of life?
- In patients with low grade glioma, can the use of circulatory biomarkers predict an early malignant transformation process?

Neuro-oncology: Summary

- We will continue to fund research in brain and spinal cord tumours; the remit is unchanged other than the inclusion of disease models as a focus (introduced for 2023 project grant call).
- We will make clear that we welcome applications in all types of brain and spinal cord tumour, and will publish data on applications received and success rates.
- We will improve feedback to unsuccessful applicants, so that they may succeed in future applications.

7 Priority area 2: Acquired brain and spinal cord injury

This theme includes both traumatic and non-traumatic brain and spinal cord injuries but excludes neuro-degenerative conditions.

Acquired brain and spinal cord injury (ABSCI) was highlighted as a research priority in 2016 due to ongoing levels of high unmet need amongst those affected, and limited availability of dedicated research funding.

Our original remit (agreed in 2016) was focused on recovery mechanisms: *‘Research into impairment-based interventions to relieve acquired brain injury, including (or ‘assisted by’) interventions to enhance plasticity and stimulation’*. The wording has been updated through further discussion and reflection, to enable a broader focus that encompasses the funding of mechanistic, diagnostic and prognostic research in brain and spinal cord injury, with the most recent incarnation set out below.

Acquired brain and spinal cord injury

We want to fund research that aims to protect or restore function in patients with acquired brain or spinal cord injury.

Within this remit, we will fund research that addresses the mechanisms of the injury, the mechanisms of the recovery process, and determinants of outcome.

7.1 About brain and spinal cord injury: the facts

- Head injury is the commonest cause of death and disability in people aged 1 to 40 years in the UK⁹.
- More than 350,000 people are admitted to hospital every year in the UK with an acquired brain injury (ABI) – including 158,000 with traumatic brain injuries (TBI), and 137,000 with stroke¹⁰.
- A further 2,500 people are diagnosed with a spinal cord injury (SCI) each year in the UK¹¹.

The number of deaths from these injuries is going down - thanks to better emergency care and, in the case of stroke, better awareness of symptoms, and availability of clot-busting drugs. This means that the population of survivors is growing ever bigger. Estimates of the numbers of people in the UK living with long-term problems as a result of an acquired brain or spinal cord injury include:

- 1.3 million with traumatic brain injury related disabilities¹²
- 1.3 million with the effects of stroke¹³
- 50,000 living with spinal cord injury¹¹

‘Time for Change’, a report by the All Party Parliamentary Group on Acquired Brain Injury (2018)¹² highlights the clinical- and cost-effectiveness of early, specialist neuro-rehabilitation but notes the inadequate and variable provision around the UK. It highlights the particular impact on children, in terms of the impact on education and life chances.

Although the Time for Change report is generally focused on neuro-rehabilitation and the care pathway, rather than research, one of the recommendations is for more research into the links between concussion and late degenerative disease.

“Acquired Brain Injury (ABI) is a leading cause of death and disability in the United Kingdom. It is a chronic condition with ‘hidden’ disabilities and life-long consequences. The excellent advances in

emergency and acute medicine mean that many more children, young people and adults now survive with an ABI, however, many of these individuals require early and continued access to neurorehabilitation to optimise their recovery and maximise their long-term potential.” Time for Change: All-Party Parliamentary Group on Acquired Brain Injury, 2018.

7.2 Review of Brain Research UK acquired brain and spinal cord injury funding

Since 2017, through our national calls, we have invested £4.3 million in research focused on brain and spinal cord injury – through 12 project grants and 4 PhD studentships. *Figure 6* shows the breakdown of these grants by disease category.

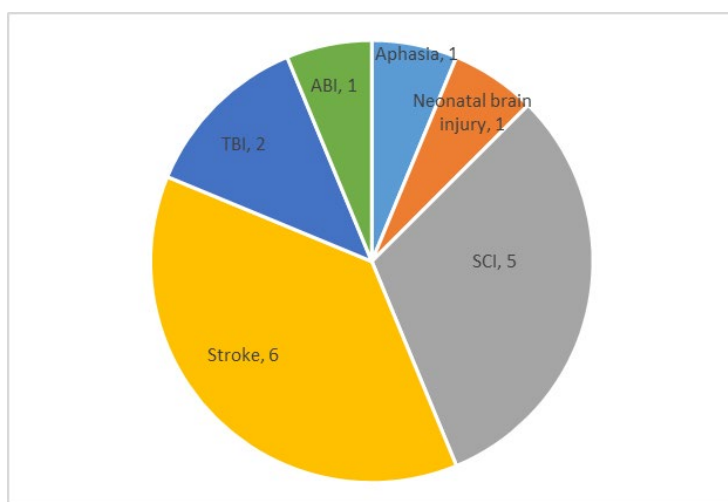


Figure 6:

Acquired brain & spinal cord injury grants awarded, 2017 to 2023

7.3 External funding environment, brain and spinal cord injury

There is a range of funders supporting research into different types of brain and spinal cord injury.

The Stroke Association is the highest profile funder of research into stroke, but their remit also includes the provision of support and information services to people affected by stroke. Their research spend in 2021/22 was £1.4m (2020/21: £1.8m).

Stroke Association funding includes Postdoctoral fellowships and Clinical-academic postdoctoral fellowships, to support Fellows ‘who plan to conduct stroke research into clinical and applied health, including social care research’ and aligned with the priorities established by the JLA Priority Setting Partnership for Stroke (2021).

Spinal Research is the UK’s leading spinal cord repair charity, with a research spend of £970k in 2022 (2021: £248k). Their aim is ‘to find an effective treatment for paralysis caused by spinal cord injury’. They have a range of funding streams including PhD studentships, basic science ‘strategy’ awards open to international applicants, translational awards aimed at addressing scientific and technical hurdles on the critical path to the clinic, ‘special emphasis’ grants for multi-disciplinary outcome-driven initiatives based on restoration of neurological function.

In TBI, funding was announced in June 2023 for a £9.5 million UK-wide research platform ‘to transform treatment of traumatic brain injury’¹⁴. Jointly funded by the Medical Research Council, the National Institute for Health and Care Research, the Ministry of Defence and Alzheimer’s Research UK, the UK-TBI Repository and data PORTal Enabling discoverY (*TBI-REPORTER*) brings together leading experts from across the UK to enable and coordinate research into TBI. The platform will include a data hub to collate and curate TBI research data at scale, a national biomarker resource, and an experimental medicine network of research-ready NHS specialist neuroscience hospitals. This new infrastructure will support, coordinate and accelerate TBI research in the UK and we look forward to following its progress and seeing how it impacts research proposals submitted under our calls.

7.4 External reports on brain and spinal cord injury research

There are three JLA Priority Setting Partnerships of relevance to this theme, two in stroke¹⁵ (*Stroke prevention, diagnosis, pre-hospital and hospital care (2021)*, and *Stroke rehabilitation and long term care (2021)*) and one in spinal cord injury (2014)¹⁶. The partnerships tease out the research questions that are important to those affected by these conditions.

Many of the questions are outside the scope of our funding, relating to primary prevention, care pathways, service provision or epidemiology. Bearing in mind our requirement for a mechanistic hypothesis, questions of relevance from the two stroke reports included questions about:

- Benefits and risks of acute treatments for intracerebral haemorrhage
- Benefits and risks of new therapies for stroke (e.g. stem cell therapy) and those that work to protect the brain from damage (i.e. neuroprotection)
- The processes causing delayed changes in brain function (neurological deficit) after subarachnoid haemorrhage caused by an aneurysm
- Effects of, and best assessments and interventions for, the range of communication difficulties in stroke
- Prevalence of fatigue, types, causes/triggers and experiences of its effects; best ways to treat and self-manage – to minimise impact on recovery and life after stroke
- Optimal time, place and amount of therapy (e.g. speech and language therapy, physiotherapy, occupational therapy) to get best outcomes for stroke survivors.
- Best intervention to improve outcomes for people with severe stroke and long-term disability, and benefits of long-term rehabilitation
- Type and intensity of treatment effective at a later stage, and whether there is a fixed time period after which no further improvement can be made.
- Type and timing of interventions to improve arm function after stroke

Again bearing in mind the requirement for a mechanistic hypothesis, potentially relevant questions from the Spinal cord injury report included the following:

- Does activity-based rehabilitation, including functional electrical stimulation coupled with physical activity and hydrotherapy, improve outcomes such as muscle function and neuroplasticity after spinal cord injury?
- Does stem cell therapy result in better outcomes after spinal cord injury and does this depend on the type of injury (e.g. acute or chronic; complete or incomplete)?
- Does chondroitinase administration after spinal cord injury result in improved repair or recovery outcomes, including improved muscle function and sensation?
- Does physiotherapy after spinal cord injury improve functional outcomes, including neuroplasticity?
- Does the timing in which corticosteroids are administered following a spinal cord injury have an effect on outcomes and recovery?
- Are baclofen or gabapentin in comparison to other drug treatments more effective in reducing spasticity and stiffening of limbs (after spinal cord injury)?

Acquired brain and spinal cord injury: Summary

- We will continue to fund research in acquired brain and spinal cord injury. The remit was updated for the 2023 project grant call and will be kept under review. The development of disease models was included as a new focus in 2023 and will be maintained.

8 Priority area 3: Headache and facial pain

Headache and facial pain was highlighted as a research priority in 2016 due to ongoing levels of high unmet need amongst those affected, combined with low levels of research funding.

We call for applications meeting the following remit:

Headache and facial pain

We want to fund research that aims to improve the management and treatment of headache or facial pain disorders.

We will fund research that addresses the fundamental causes, mechanisms, diagnosis or treatment of headache and facial pain.

We will also fund the development of models that enhance this theme and facilitate translation. Models may be in vivo or other 3D models, and must support the future testing of a mechanistic hypothesis.

8.1 Headache and facial pain: the facts

- Headache disorders are the cause of more than three quarters of all neurological years lived with disability, despite the fact that neurological diseases include epilepsy, dementia, Parkinson's disease, multiple sclerosis and motor neurone disease¹⁷.
- **Migraine** is the most common *disabling* headache disorder, estimated to affect around 11 million people in the UK¹⁸. There are an estimated 190,000 migraine attacks occurring every day in the UK¹⁹.

Because of its prevalence and severity, migraine is the fourth leading cause of disability in the UK, measured in terms of years lived with disability (YLD)²⁰. In the 15 to 49 year age group, migraine is the top cause of YLDs.

For many of those affected, the main feature of migraine is a painful headache but the disorder is associated with a wide range of other symptoms, including disturbed vision, sensitivity to light, sound and smells, feeling sick and vomiting.

- **Tension-type headache** (TTH) is the most common primary headache disorder, but significantly less disabling.
- **Cluster headache** is an excruciatingly painful headache disorder estimated to affect around one in 1,000 people²¹, equivalent to around 65,000 in the UK. Described as one of the most painful conditions known to man, the intense pain is often reported to give rise to suicidal thoughts, hence it being known as the *suicide headache*. Attacks occur in clusters for a period of several weeks or months, then remit, leaving the patients pain free for several months or even years, only for the attacks to recur. The unpredictable, intense nature of the pain impacts heavily on the lives of those affected, causing multiple admissions to hospital, restricting people's lifestyles and often leading to unemployment.
- **Trigeminal neuralgia** is described as a '*sudden, severe, brief, stabbing pain occurring in attacks lasting at the most a few seconds usually only on one side of the face and provoked by light touch*'. Like cluster headache the pain is described as the '*worst pain known to man*'. Attacks are often described as being like an electric shock, which can literally bring people to their knees. Attacks may last for a few seconds or occur in 'volleys' – multiple bursts of pain in quick succession – lasting several minutes. Frequency of attacks can vary from a few times a month to several times each day. For most sufferers, the condition is progressive and will worsen over time. Around 5,000 people are newly diagnosed with trigeminal neuralgia every year in the UK²².

- The direct healthcare costs of migraine alone are estimated at around £1bn a year in the UK, and the indirect costs due to lost productivity are estimated at just under £8.8bn per annum²⁰.

Despite this enormous burden of disability, research into headache has not attracted substantial research investment. This has severely limited progress in research and treatment of headache disorders.

“Headaches are an unglamorous disability - the Cinderella of the medical profession, under-rated and often ignored”, Stephen O'Brien MP, from 'Headache Disorders - Not Respected, Not Resourced. A Report of the All-Party Parliamentary Group (APPG) on Primary Headache Disorders', 2010²³.

8.2 Review of BRUK headache and facial pain funding

Since 2017, through our national calls, we have invested £1.6 million in research focused on headache and facial pain (HFP) – through three project grants and five PhD studentships, with the breakdown by disease area shown in *figure 7*, below.

We typically receive few applications in HFP and, considering this, they have generally fared reasonably well.

As shown earlier in this document (*figures 3 and 4*), we received only one studentship application in HFP in the most recent call (out of 20 applications), and 11 preliminary project grant applications (out of 77 applications). The studentship application was not short-listed; three of the project grant applications were short-listed and one of these was ultimately funded. Of the non-shortlisted applications, concerns around fit with remit, relevance and phenotyping were common. There was also concern about the relevance of disease models.

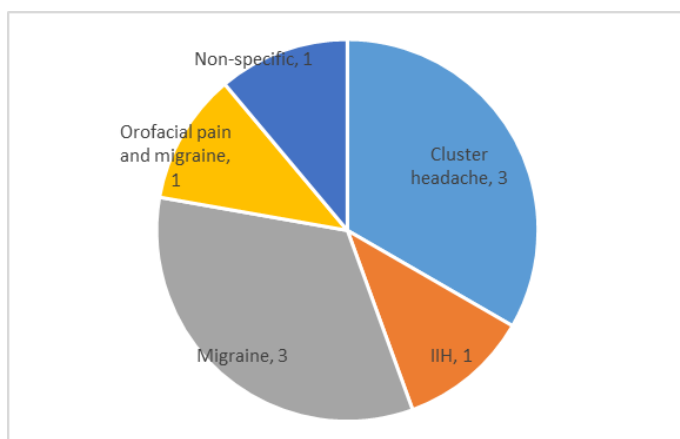


Figure 7: Headache & facial pain grants awarded, 2017 to 2023

Total value: £1.6m

- **We will increase our efforts to promote our funding calls to the headache community to drive up the number of applications, and will improve the feedback given to all applicants to help them succeed in future applications.**

8.3 Funding landscape

The Migraine Trust is the leading dedicated funder of headache research in the UK. They fund research seeking to *‘improve the management and treatment of migraine and to find a cure’*. They reported research expenditure of £66k in 2021/22, towards two PhD studentships (2020/21: £123k). In 2023 they advertised for applications to fund two one-year fellowships, through which they aim to *‘support the development of early career clinicians or scientists to conduct clinical or fundamental scientific research in headache disorders’*.

8.4 External reports on headache and facial pain

The 2010 APPG on Primary Headache Disorders²³ states that when they met to review UK spending on headache research, there was none to identify and that *'the funding bodies could not even be bothered to turn up and explain the issue'*. In the report, Dr Richard Hargreaves comments on how the general level of research into headache disorders appears to be 'dwindling' after the breakthroughs of the 1990s.

The report set out a number of recommendations for the way forward in headache research, including a recommendation for basic research in the mechanisms of headache disorders in order to identify and characterize new targets for treatment, and a recommendation to co-ordinate translational research in headache, utilising the opportunity presented by the NHS to achieve this. It also recommended the establishment of an MRC Headache Unit. Professor Peter Goadsby concludes the report saying *'Headache is neither impossible nor intractable and with a small investment can be an area in which the UK leads the world and provides value to patients and to society. Ignoring a problem that effects more than ten million people cannot be correct, nor can it be a strategic option for the future.'*

Headache and facial pain: Summary

- We plan to continue funding research in headache and facial pain; the remit is unchanged other than the inclusion of disease models as a focus, introduced for the 2023 project grant call.
- We will promote the calls more widely to the headache community to drive up the number of applications received under this theme.
- We will improve feedback to unsuccessful applicants, to help them succeed in future applications.

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