Institution: Newcastle University

Unit of Assessment: 4 - Psychology, Psychiatry & Neuroscience

a. Overview

Research activity in the UoA4 return addresses our core mission to undertake high quality basic neuroscience that translates into real world application, commercial opportunity and patient benefit. Our research is reported under three broad research themes: Systems Neuroscience, Clinical Neurosciences and Comparative Cognition and Behaviour. In our clinical research we have a particular interest in the neurological and psychiatric health challenges faced by the older person, understanding their causes and impacts, and developing effective approaches to treatment. The translational aspects of a number of our programmes are underpinned by research employing a wide variety of animal models, notably the non-human primate for which we are one of Europe's leading centres. Key to the delivery of our programmes is our strategic mix of basic and clinical academics, administered through two of the Faculty of Medical Sciences' multi-disciplinary institutes: the Institute of Neuroscience (IoN) which provides a focus for neurobiological, behavioural and clinical neuroscience research and the Institute for Ageing and Health (IAH) which underpins Newcastle's pre-eminent position as a centre for excellence in ageing and agerelated disease. Substantial investment in our Institutes has provided the high quality infrastructure necessary to support our research programmes which have seen marked growth, with the value of active awards rising from £18.4M (2007/8) to £44.3M (2012/3). Collaboration is central to our multidisciplinary research. Many UoA4 researchers are closely linked with our NHS partners, notably Newcastle upon Tyne Hospitals NHS Foundation Trust and Northumberland, Tyne and Wear NHS Foundation Trust. We have strong links with researchers in UoA1 (Clinical Medicine), notably in mitochondrial disease and genetic medicine, and in UoA2 (Public Health, Health Services & Primary care), in areas of neurodevelopmental disorders and applied health research. We also work closely with the Faculty of Science. Agriculture and Engineering in the fields of assistive technologies and neural device development (UoA13 - Electrical and Electronic Engineering, Metallurgy & Materials) and animal welfare (UoA6 – Agriculture, Veterinary & Food Science). Other important organisational groupings that facilitate our working across the University include the £16.6M Newcastle NIHR Biomedical Research Centre (BRC) in Ageing and Chronic Disease, the £4.75M Newcastle NIHR Biomedical Research Unit (BRU) in Lewy Body Dementia, and the Centre for Behaviour and Evolution (CBE). This broad network of collaboration is essential in achieving our goal of effective research translation.

b. Research Strategy

Summary of Research Strategy: Our strategy since the RAE2008 has focussed on developing and investing in three areas of recognised expertise and excellence: Systems Neuroscience (sensory, motor and cognitive systems), Clinical Neurosciences (Lewy Body Dementia, stroke and affective disorders) and Comparative Cognition and Behaviour. Our over-arching strategic aim has been to address key scientific and health challenges, with particular emphasis on clinical neuroscience that applies to an ageing population, and research that has a strong translational focus whilst delivering high quality basic research discovery. We have made significant progress in realising this aim through the following strategic actions: (i) expansion of our research capacity through development of our staff and key appointments, (ii) development of our infrastructure and research capability through strategic awards and investment, (iii) enhancing our work studying behaviour and neural systems from a comparative perspective, particularly using the non-human primate and (iv) enhancing our translational activity, particularly by building links with the NHS and NIHR. Examples of the latter include the award in 2012 of the NIHR BRC (in which the Ageing Brain is a core theme) and the NIHR BRU, and a capital award from the Wellcome Trust to create a Centre for Translational Systems Neuroscience. In delivering our strategy we aim to enhance the interactions between researchers engaged in basic science and clinical neuroscience, both within our Institutes and with external groups, and to align with the University's core mission of 'Excellence with a Purpose' and its strategy of addressing the Societal Challenge of the needs and opportunities relating to both healthy and unhealthy ageing - Newcastle Initiative on Changing Age. Going forward, we aim to implement our translational research more effectively through these new research structures and via our recently funded NIHR Academic Health Science Network.

(i) Systems Neuroscience: Our main aims for this theme are to elucidate the fundamental neural mechanisms of vision, hearing, movement, language, attention and affect, and to understand the organisation of neural networks and how their disruption may underlie disease. Our goal is to





translate basic science knowledge into innovative treatments for neurological and psychiatric disorders. A particular strength is our ability to integrate discoveries across organisational levels, from *in vitro* and *in vivo* studies of network dynamics, to non-invasive neuroimaging and psychophysics, as well as across species, from rodents to humans. The non-human primate (NHP) is a key animal model for probing fine motor control, visual and auditory perception, and higher cognitive functions relevant to humans and, as the UK's largest group using macaques for neuroscience research, we remain committed to translating discoveries from NHP research into clinical applications.

Main Developments since 2008: We have significantly developed our programme of work utilising the NHP model, appointing **Petkov** to strengthen research in auditory processing and language, investing in infrastructure, upgrading our NHP-dedicated MRI scanner to multi-channel parallel imaging and expanding our MR physics support (Wellcome Trust Equipment Grant, £453K). Translational work in epilepsy has been enhanced by the appointments of **Trevelyan** (rodent and human recording) and **Whittaker** (clinical neurophysiology), who also strengthens our work on motor disorders. Support for multi-disciplinary neuroscience has come from our <u>Wellcome Trust 4-year PhD programme in Systems Neuroscience</u> (first cohort 2008) which specifically recruits students from backgrounds in physical sciences, mathematics and engineering.

Key Achievements: Our discoveries in auditory and visual neuroscience exemplify our multilevel approach to understanding brain function. Using functional MR imaging (fMRI) in the awake monkey, we showed how the midbrain inferior colliculus is organised in orthogonal tonotopic and periodotopic dimensions (Griffiths, Rees, Petkov, Thiele, Sun; Nat Neurosci). Parallel fMRI studies in man revealed how auditory processing is organised at cortical levels (Griffiths; J Neurosci), which was confirmed by direct intra-operative recordings from human auditory cortex in response to pitch (Griffiths; Current Biol). At the level of more complex sound processing, Petkov identified a voice region in macaque auditory cortex using fMRI (Nat Neurosci) and used MRIguided electrophysiology to show that neurones in this area have high selectivity for communication signals (Current Biol). Using the visual system as a model, Thiele used multi-electrode, multiareal recording in the macaque to demonstrate the mechanisms of perceptual learning and attention (J Neurosci), and combined this with local drug delivery to determine the mechanisms by which cholinergic and NMDA receptors mediate cognition (Nature; Neuron). Our aim of understanding neural networks and their disruption in disease is exemplified by our work in motor systems and epilepsy. Both NHP and human studies have explored normal motor pathways and their reorganisation following lesions or progressive neurological disorders. For example, Baker defined the role of the reticulospinal tract in hand control (J Neurosci) and showed that strengthening of this pathway after a corticospinal lesion may underlie the pattern of weakness and spasticity seen following stroke (Brain). Our studies of neural networks have focussed both on oscillatory activity and how it becomes disrupted in neurological illness, and on the neurochemical properties of networks that underlie psychopharmacological action of drugs. Notable are our studies of human epileptic cortical tissue, both in vivo (Trevelyan; Brain, Nat Commun) and in vitro (Cunningham; PNAS) that have demonstrated the importance of inhibitory restraint in regulating seizure propagation and the role of non-synaptic mechanisms underlying interictal discharges.

Future Plans: In delivering high impact basic science we aim to resolve the networks underlying sensory, motor and cognitive systems by exploiting techniques to achieve ever finer resolution and control, including applying optogenetics in awake NHPs. We aim to translate these discoveries into novel therapies based on network modulation enabled by the Centre for Translational Systems **Neuroscience** which provides new NHP labs and experimental resources for human studies. Planned academic appointments linked to the Centre will enable us to apply the NHP model to new areas of systems neuroscience. Recently funded projects that support this translation include: studies on subcortical networks controlling movement after stroke (Baker; Wellcome Senior Fellowship £2.47M); the role of attention in mechanisms of cortical adaptation in primates (Petkov, Vuong; BBSRC £576K); anti-epileptic inhibitory mechanisms in neocortex (Trevelyan, Racca; MRC £760K); and the use of high density (4096 electrode) arrays to study spatio-temporal coding in the retina (FP7 RENVISION, Sernagor). Building on our links with engineering, we will expand our work developing novel therapeutic and diagnostic technology, including a multi-channel EMG electrode for muscle imaging (Whittaker; EPSRC; £583K) and an implant for controlling cortical dynamics in epilepsy using optogenetics, funded via a recent Wellcome-EPSRC Innovative Engineering for Health Award (Baker, Cunningham, Ingram, Trevelyan, Whittaker; £10M 2013-20).



(ii) Clinical Neurosciences: This theme focuses on three disease areas in which we have wellestablished track records: the <u>Lewy Body Dementias</u> (LBDs: both dementia with Lewy bodies (DLB) and dementia of Parkinson's disease (PD)), <u>Stroke</u>, and <u>Affective Disorders</u> (particularly bipolar disorder and late-life depression). The broad aim of our clinical research is to improve the management of patients through early and accurate diagnosis, improved understanding of pathophysiology, disease course and potential modifiers, and development of novel treatments, including stratified medicine approaches. A particular strength of our clinical groups is their multidisciplinary nature. For example, our LBD research is led by NIHR Senior Investigators in Old Age Psychiatry, Movement Disorder Neurology, Clinical Pharmacology, Neurogenetics, and Gerontology. Our experimental medicine stroke research constitutes a major component of the 'Ageing Brain' theme of the NIHR BRC in Ageing and Chronic Disease, and also has strong links with investigators returned in UoA2 for trial design, applied health research and service implementation.

Main Developments since 2008: Our strategic focus on LBD is aligned to the National Dementia Strategy and to the Prime Minister's Dementia Challenge, and the award of the BRU in Lewy Body dementia has enabled us to expand our programmes in imaging, biomarkers and therapeutics in clinically well-defined LBD cohorts through a number of strategic appointments. For example, the appointment of **White** (Chair, Interventional and Diagnostic Neuroradiology) builds upon our investment in neuroimaging, with a view to developing multi-centre commercial and industry-led interventional studies. At the same time we have concentrated our clinical neurosciences research on a multi-disciplinary research campus, the **Campus for Ageing and Vitality** (see Infrastructure d (ii)), where investment in a new Psychiatry Research Unit and Biomedical Research Building has provided new opportunities across the clinical neurosciences theme.

Key Achievements: Our achievements span aspects of diagnosis, disease characterisation and treatment. Examples from the three clinical areas include: LBD: In improving diagnosis we showed that dopaminergic SPECT differentiates DLB from Alzheimer's disease (AD) with >80% accuracy (McKeith; Brit J Psych; confirmed by a clinico-pathological correlative study, Attems; Brain), and led an industry-funded Phase III study (GE Healthcare; 40 sites, 10 countries) which validated the findings in a large international cohort. Consequently dopaminergic imaging is now recommended by NICE as the investigation of choice for resolving diagnostic uncertainty in DLB. Using cases imaged during life and material from the MRC-funded Newcastle Brain Tissue Resource we undertook the first autopsy validation of medial temporal lobe atrophy as a diagnostic marker for AD, and demonstrated a link with underlying tau pathology (Kalaria, Mukaetova-Ladinska; Brain). Both findings are included in the European Federation of Neurological Societies' Guidelines for dementia. Stroke: Clinical management has been a key focus for our stroke research, in which we coordinated international randomised control trials (RCTs) to assess the value of early surgery in managing intracerebral haematomas (STICH II; Mendelow; Lancet) and the use of coated coils for cerebral aneurysm therapy (HELPS; White; Lancet), and completed the largest rehabilitation RCT of botulinum toxin in stroke to determine impact on arm function (Rodgers, Ford; Stroke). Linking with our LBD work, we demonstrated the relationship between hippocampal atrophy and cognitive function in delayed post-stroke and aging-related dementias (Allan, Polvikoski, Kalaria; Stroke) and determined the pathological diagnosis and long term incidence of dementia in older stroke survivors (Allan, Thomas, Polvikoski, Kalaria; Brain). Affective Disorders: In exploring the mechanisms underlying bipolar symptoms as a route to therapy, we showed that a glucocorticoid receptor antagonist can lead to sustained improvement in symptoms (e.g. spatial working memory; Watson, Ferrier; Biol Psychiat), and developed novel MR imaging and spectroscopy to determine lithium distribution and its effect on grey matter volume (Cousins (MRC Clinician Scientist Fellowship), Ferrier; Biol Psychiat).

Future Plans: Our over-arching aims are to improve early disease diagnosis and introduce novel therapies into clinical practice. In <u>LBD</u> we will focus on improved diagnosis and demarcation of LBD subtypes as a basis for improved clinical pathways, in line with the priorities of the Ministerial Advisory Group for Dementia Research. Via our <u>NIHR Programme Grant</u>, DIAMAND-Lewy (**Thomas, McKeith, Burn, Taylor, Allan**; £1.66M) we will validate assessment tools to facilitate timely and accurate diagnosis and determine the feasibility of introducing a 'management toolkit' in secondary care. To improve diagnostic accuracy we will explore novel biomarkers (e.g. gait) and work with industry to validate new imaging tracers. We have initiated an <u>NIHR-HTA</u>-funded 21-centre study to determine the clinical effectiveness of the cholinesterase inhibitor donepezil for



treatment of early PD dementia (MUSTARDD-PD; Burn, £2.08M). Funding from the Michael J Fox Foundation (£813K) will enable us to establish the best instrument to assess cognition in PD in therapeutic studies. In Stroke our focus will be on addressing areas of improved assessment of suspected stroke, hyper-acute stroke treatment and interventional neuroradiology, and assistive technology and therapy for motor rehabilitation. This will build on projects including our NIHR-HTA programme on Promoting Effective And Rapid Stroke care (PEARS; Ford, Rodgers, White, Price; £1.92M), our HICF project 'Limbs Alive' to improve post-stroke recovery via interactive video gaming (Eyre; £1.62M), and our NIHR-HTA-funded stroke rehabilitation trials: RATULS (Robot Assisted Training for the Upper Limb after Stroke; Rodgers, Ford, Eyre, Rochester; £3.09M) and EXTRAS (evaluating an extended rehabilitation service; Rodgers, Ford; £1.65M). We will expand our work in early intervention RCTs through an on-going phase III thrombectomy trial (PISTE; White £388K for start-up phase) and phase II pan-European RCT of a novel stroke thrombectomy device (STABILISE; White £650K). In Affective Disorders we will build on the outcomes of the MRC-funded Bipolar II cohort in defining core cognitive deficits and pursue these as therapeutic targets in studies such as our NIHR/MRC EME trial of anti-glucocorticoid augmentation of antidepressants (ADD; Ferrier; £627K). Building on our work on cerebral blood flow and intensive blood pressure lowering, the VALUED interventional (Thomas; NIHR £141K) and BRILIANT Mood (Thomas; MRC £288K) studies will investigate vascular substrates for depression in older people and their relationship to cognitive impairment.

(iii) Comparative Cognition and Behaviour: The aim of this theme is to increase understanding of the cognitive and neural mechanisms underpinning behaviour in an evolutionary context. Our work ranges from how visual information drives behaviour, to complex decisions concerning cooperation and life choices. The strength of our comparative approach lies in the capacity to select appropriate and novel models, and to demonstrate how behavioural processes generalise across species. As well as having relevance to individual species, this helps us understand human behaviour and, consequently, key issues in society and human health. The University Research Centre for Behaviour and Evolution (CBE), founded in 2007, provides an organisational basis for this theme and facilitates cross-Faculty collaboration. It is one of the largest groupings of its kind in the UK, supporting 12 academic staff reported here and 6 others in UoA6 and UoA7.

Main Developments since 2008: Along with the creation of the CBE we have strategically expanded our capacity and capabilities, making appointments in animal behaviour and cognition (Skelhorn: predator cognition / evolution of prey defences; Price (Early Career Researcher (ECR)): tool use and problem-solving in birds/primates), and in areas of human neuroscience and cognition (Mullally (ECR): spatial cognition; Gallagher (ECR) (also Clinical Neuroscience): neuropsychology of working memory). These appointments have increased the opportunities to transfer techniques and ideas across traditional discipline boundaries. We have successfully responded to national priorities, notably the UK Insect Pollinators Initiative in which Wright holds two grants (£760K), and have applied our research to address animal welfare issues, both in relation to agricultural species (BBSRC and DEFRA funding) and to NC3Rs priority areas for laboratory species (current portfolio of NC3Rs funding: £632K). We have actively fostered interdisciplinary projects through allocation of PhD studentships and strategic resourcing of junior staff whose work bridges several systems (e.g. Skelhorn; birds, insects, humans; Jennings; deer, rodents, humans; Price: humans, great apes). We have also started two research Master's programmes (MRes Animal Behaviour in 2010, MRes Evolution and Human Behaviour in 2012) to underpin our integrated PhD programme.

Key Achievements: Our comparative approach has enabled us to demonstrate how some behavioural attributes normally considered the domain of 'higher' species are more widely expressed. An example of this is the demonstration of how stress and environment can determine pessimistic or optimistic cognitive biases in a range of species including, for the first time, demonstrating affective state in invertebrates (**Wright, Bateson, Gartside**; *Current Biol*). We have shown how environmental and stress factors have long term programming effects on cognition, both in a laboratory setting with rodents and in a field setting with wild populations of starlings. These studies have informed new evolutionary models of affective states, such as depression and anxiety (**Bateson, Nettle**; *Current Biol*). We have exploited the comparatively simple nervous systems of insects to model several behavioural processes. For example, our studies on the impact of nectar on bee nutrition and behaviour have shown that caffeine can influence memory for reward (**Wright**; *Science*), while olfactory memory can be modulated by cholinergic pesticides (including



neonicotinoids) through an action on the mushroom body (**Wright**; *Nat Commun*). This research highlights the potential ecological impact of these compounds on bee foraging behaviour and contributes to the debate surrounding the widespread use of pesticides. **Skelhorn**'s work has also shown how the cognitive abilities of predators drive the evolution of natural prey defences, including masquerade (*Science*) and warning signals (*Proc Roy Soc B*). Our human studies span core neuropsychological processes (e.g. spatial cognition) to complex social behaviours. Work on co-operative behaviour has explored the potential neurobiological determinants (**Nettle**; *PNAS*) and demonstrated the impact that the stimulus of 'watching eyes' has on social co-operation in real world settings. This work has had impact on crime prevention and controlled studies have shown strong effects on reducing anti-social behaviour such as theft (**Nettle, Bateson**; *PLoS One*).

Future Research Plans: We aim to exploit the transfer of ideas and concepts across species and disciplines to determine the neural systems and cognitive processes that drive behaviour, studied both in laboratory controlled and real world settings. For example, we will build on our expertise in measuring patterns of cognitive development and decline to develop novel biomarkers of animal welfare (including telomere dynamics) applying these, for example, to the impact of cumulative procedures on laboratory macaques (**Bateson, Thiele, Rowe**; <u>NC3Rs, £485K</u>) and the effect of agricultural practice on chronic stress in livestock (**Smulders**; <u>BBSRC</u> £378K). We will capitalise on opportunities arising from our recent appointments to undertake new cross-disciplinary and cross-species research, an approach that will generate novel discoveries that can have significant societal impact. For example, combining our work on visual cognition in predation (**Rowe, Skelhorn**) with psychophysics of stereo vision (**Read**), has recently led to a new programme on 3D vision in the praying mantis (<u>Leverhulme Research Leadership Award</u>, £961K), that will contribute novel algorithms that may be applied to robot vision and 3D display technology.

c. People

i. Staffing strategy and staff development

Our staffing strategy has been to strengthen and grow our core research themes through the development of our existing academic and research staff and by appointing outstanding individuals who bring added value or address unmet research needs. Since 2008 we have appointed 10 staff (6 to their first academic position) with a balanced distribution of internal (**Trevelyan, Whittaker, Gallagher**), external UK (**White, Rochester, Skelhorn**) and non-UK (**Attems, Petkov, Mullally, Price**) appointments. We aim to recruit the best and are internationally competitive in attracting and retaining high quality researchers, evidenced by the fact that 21/55 of our returned staff and 73% of our post-doctoral researchers are originally from outside the UK. Career development of our staff is reflected in the fact that 14 returned staff have been promoted since 2008.

Systems Neuroscience: Our strategy has aimed to consolidate and expand our strength in NHP systems neuroscience, and to support our translational research. We have made four key appointments focussed on: NHP auditory systems neuroscience and neuroimaging (**Petkov** (appointed, 2008; promoted to Reader, 2013) and Baumann (Faculty Fellow)); clinical neurophysiology in motor systems and epilepsy (**Whittaker**, Clinical SL, 2013), and networks in epilepsy (**Trevelyan**, SL, 2012), and are making further appointments in NHP neuroscience linked to capital investment. Two strategic appointments in Electrical and Electronic Engineering (UoA13) support our work in neuroengineering: Degenaar (Reader in Neuroprosthesis) and Nazarpour (Lecturer, Brain-Machine Interfaces). The promotion of **Rees** (Chair, Auditory Neuroscience, 2013) and **Sernagor** (Reader, Developmental Neuroscience, 2011) reflects their excellence in their fields.

Clinical Neurosciences: We have made four strategic appointments in key areas that underpin our clinical programmes. **Rochester** (Chair, Human Movement Science, 2008) has developed a Gait Laboratory to provide novel approaches for our programmes in LBD and stroke, e.g. gait as a biomarker for cognitive decline; **Attems** (Reader then Chair, Neuropathology, 2009) was recruited to implement high-throughput quantitative assessment of neuropathological lesions; **White** (Chair, Interventional and Diagnostic Neuroradiology, 2012) builds on our investment in neuroimaging with new programmes in interventional neurovascular procedures; and **Gallagher** (ECR Lecturer, 2013) was appointed to develop detailed neurocognitive measures in our work in affective disorders and dementia. The departure of O'Brien to Cambridge in 2012 provided the opportunity for **Taylor** (<u>Wellcome Trust Intermediate Clinical Fellow</u>) to assume leadership responsibilities in old age psychiatry and imaging and to raise his national profile via multi-centre projects. **Rodgers** (Chair, Stroke Care, 2008) and **Thomas** (Chair, Old Age Psychiatry, 2013) were promoted for their respective leadership in stroke rehabilitation and late life depression linked to neuropathology.



Comparative Cognition and Behaviour: Our strategy has been to consolidate and grow the CBE as a centre of excellence for comparative cognition and behaviour. To expand opportunities for interdisciplinary research we have recruited staff with complementary approaches: **Price** (ECR Lecturer, 2012) uses social learning in great apes to understand child cognitive development; **Skelhorn** (Lecturer, 2013) translates work on taste learning in predators to study the emotion of disgust; and **Mullally** (ECR Lecturer, 2013) studies how spatial cognition and mental time-travel underpin development of memories. To support the integration of staff using insect model systems, three staff joined IoN from the science faculty (**Rind, Wright,** Simmons). Personal chairs were awarded to **Bateson** (Ethology, 2012) and **Nettle** (Behavioural Science, 2011) and Readerships awarded to **Rowe** (2008) and **Wright** (2011) reflecting pre-eminence in their respective fields.

Support and Development of Staff: We have a strong institutional commitment to career advancement and proactive development schemes exist to support both ECR and established researchers. ECR development focuses on: (i) supporting the successful establishment of newly appointed staff through mentorship and targeted resource allocation, and (ii) career pathways to support talented postdoctoral associates aspiring to independent investigator posts. We place considerable importance in fellowships to support our most promising researchers both at ECR and established levels (see Section d for key fellowships held in the REF period). The development and research support needs of individual academic staff are identified through the annual Performance and Development Review (PDR) conducted by the Institute Directors. Newcastle was one of the first universities in Europe to be awarded the HR Excellence in Research Award (2010) for its policies on PDR and for championing the Concordat to Support the Career Development of Researchers. This support is effected through the Faculty's flagship Career Pathways Scheme, the three main aims of which map closely with those of the Concordat: active career management, continuity of employment and knowledge exchange. Activities at 3 months (induction), 9 months (career awareness workshop) and 2 years (career planning workshop), complement the annual PDR in career planning for all ECR. We place high priority on the retention of our skilled researchers and over the REF period 19 have received up to 6 months funding to bridge gaps between grants. We have been successful in attracting international fellows, e.g. Kari Schroeder (USA: NSF Fellow) to work on determinants of cooperative behaviour in humans (PNAS) and Julieta Sztarker (Argentina; Marie Curie IIF) to work on collision sensing in locusts (J Exp Biol).

Our translational research is underpinned by the strong integration of clinical researchers (21 of those returned are clinical) and by well-developed clinical career pathways. Newcastle has pioneered integrated management of clinical academic career paths, and structured mentorship organised at faculty and institute level is aimed at ensuring effective career progression. Medical student academic activity (intercalation, vacation studentships, elective opportunities) is supported by external funders, including the <u>Wellcome Trust</u> and <u>Academy of Medical Sciences</u> through an INSPIRE programme and by an endowment from the Barbour Trust (£1M). Newcastle launched the first Academic Foundation programme in the UK and has an integrated programme for the development of potential clinical fellowship applicants at both PhD and intermediate level. Examples of successes over the REF period include: <u>MRC Clinician Scientist Fellowship</u> (**Cousins**), <u>NIHR Career Development Fellowship</u> following ACL (Basu), <u>NIHR Doctoral Research Fellowship</u> (Burton), <u>Guarantors of Brain Clinical Research Training Fellowship</u> (Thouin), <u>Parkinson's UK Research Fellowship</u> (Archibald) and a fellowship on a <u>Wellcome Trust Translational Medicine and Therapeutics (TMAT)</u> <u>Programme</u> hosted by Newcastle (Jaiser).

Athena SWAN Strategy: We are strongly committed to equality and fairness and to the objectives of Athena SWAN. The University is a signatory to the Athena SWAN Charter, was granted a Bronze award in 2009 and aims to achieve Silver status by 2015. Both IoN and IAH will apply for Silver status in 2014 and have established steering committees chaired by **Rowe** (IoN) and Jagger (IAH; UoA2). **Burn** is an Athena SWAN Judging Panel member and chairs the Faculty Equality and Fairness Steering Group. We also aim to achieve a work-life balance, ensuring staff are supported when there is a need to take career breaks. In returning to work after maternity leave we have a programme of 'Keep in Touch Days' and discuss working arrangements to suit child care.

ii Research Students

Programmes: We support postgraduate programmes which provide training across a broad range of basic science and clinical neuroscience. Over the assessment period the number of students



registered for a PhD has increased (2008: 49; 2012: 82) with 134 PhD completions. To ensure high quality graduates, since 2008 the entry requirement for PhD has increased to include both an excellent first degree (at least 2.1) and a relevant Master's degree (or equivalent). Three MRes programmes, largely delivered by staff within the unit, feed into our PhD programme: MRes in Neuroscience; MRes in Animal Behaviour; MRes in Evolution and Human Behaviour. In 2008 we were awarded a Wellcome Trust 4-year PhD Programme in Systems Neuroscience that has an intake of 3 students/year and will run for 6 intake years (value: £2.74M). We are also major partners in the BBSRC Doctoral Training Partnership in collaboration with Liverpool and Durham (started 2012) and the Newcastle Wellcome TMAT programme. Our Research Council-funded Newcastle Centre for Brain Ageing and Vitality has funded 17 students since 2008, and the NIHR BRU has funded 15 studentships in its first 2 years of operation. Our NIHR-funded students are part of Newcastle's NIHR Training School (Director: Jones, UoA1) which provides career advice and mentorship. Over the REF period 16 clinicians have held an NIHR ACF post or PhD position in the unit's research areas. We also deliver research-led teaching and research projects for the Doctorate in Clinical Psychology (intake 14/year). This programme was commended by a joint HCPC/BPS visit in 2012 for its clear strategy for programmatic research which brings together students and trainees at different levels, with opportunities to work on larger research projects under expert research supervision. Funding for PhDs comes from RCUK, Wellcome Trust and many charities (e.g. Parkinson's UK; Alzheimer's Research UK), and strategic allocation of matching funding has been used to support many studentships, particularly in our crossdisciplinary research. Examples include: comparative work on tool use in crows and orang-utans (Price, Smulders) and using mantids as a model of 3D vision (Rowe, Read, Rind). Over the REF period 8 PhDs have involved full or part (e.g. CASE) funding from industry (e.g. GSK; Organon; Servier; BSkyB). In attracting high quality students we actively encourage placements for undergraduates (and post-16 students under the Nuffield Science Bursary Scheme). IoN also runs a Research Summer School involving talks, laboratory visits and a project, which in 2012 attracted 22 participants (13 non-UK).

Progression, Support and Integration: Postgraduate Researchers (PgRs) in this UoA are fully integrated in its research culture and are encouraged to engage with the research environment beyond their immediate supervisors. Two independent progression panel members (Fellows of the Graduate School) meet the PgR annually to monitor progress and provide advice. PgRs are encouraged to attend University-run careers and skills training courses, and to contribute to undergraduate teaching in order to develop transferable skills. PgRs are expected to present at national and international meetings and funding is available to support this. A bi-lateral PhD Exchange Programme with Leipzig ('From signal to behaviour') funded from Germany (€485,000, awarded 2011; Newcastle lead Alter) has enabled PgRs to spend time developing their projects in our partner institution. PgRs participate in an annual Institute poster event as well as the wider North East Postgraduate Student Conference, which attracted 380 PgR delegates from all northern universities in 2012. In IAH an annual student retreat (a 2-day fully funded event in the Lake District) provides an informal setting for student feedback and encourages team building. It was highly commended by a recent Quality Assurance and Enhancement Framework assessment. Our PgR Committees meet monthly to plan social and research-based activities, and members of these committees sit on the staff Postgraduate Committee where any issues are discussed. Results of the 2013 PRES show that PhD students in the unit expressed a high level of satisfaction with the experience of their study (question 17a: 93% positive). Our PgRs contribute directly to the research productivity in the unit, with 39% of REF submitted outputs co-authored by our PgRs. In addition, many of our graduates have moved to internationally leading labs, including Boyden Lab at MIT (Harbaljit Sohal), Donoghue Lab at Brown University (Jonas Zimmermann), and RIKEN Brain Sciences Institute (Vasileios Glykos), with many retaining collaborative links.

d. Income, infrastructure and facilities

i. Research Income

Our diverse portfolio of funding reflects our broad programmes of research, from basic science to clinical and applied implementation. Research grant success has seen a year-on-year increase in income and current total grant award value is £44.3M: our success rate for project grants submitted to RCUK, NIHR and Wellcome Trust over the REF period is 35%.

Strategic Awards and Long Term Programmes: Central to our long term research plans have been a number of core strategic awards. The NIHR BRU in Lewy Body Dementia (£4.75M, 2012)



and the 'Ageing Brain' theme of the NIHR BRC in Ageing and Chronic Disease (£16.6M, 2012) provide important funding underpinning our clinical research programmes, allowing us to expand our portfolio and enabling capacity building by appointing researchers to new project areas. Our work in age-related disease also receives funding through the MRC Centre for Brain Ageing and Vitality (Co-I: Kalaria; £4.34M; 2008-13). Mendelow's programme of RCTs on surgical interventions for intra-cerebral haemorrhage has been supported both by MRC (STICHII; £1.49M; 2006-13) and NIHR (STITCH-Trauma; £2.16M; 2009-14). As part of a Faculty-wide programme in toxicology, the Health Protection Agency sponsors our work on identifying the neurotoxicological basis of chronic diseases (£1.11M; Morris). Fellowships are key to supporting a number of long term programmes of our researchers, including: Griffiths' work on auditory cognition (Wellcome Senior Clinical Research Fellowship, renewed 2012, £1.02M); Baker's work on motor pathways and post-lesion plasticity (Wellcome Senior Research Fellowship, renewed 2013, £2.47M); Taylor's work on attention and cognition in LBD (Wellcome Intermediate Clinical Fellowship, 2010-13, £573K); and Read's work on neuronal mechanisms of stereo vision (Royal Society University Research Fellowship). Other key personal research awards include five NIHR Senior Investigator awards (Ford 2008-17; Rodgers 2008-12; McKeith 2008-17; Burn 2010-14; Ferrier 2010-15).

Targeted Initiatives: We have had notable success in responding to targeted initiatives which, in part, reflects the strength of our multi-disciplinary teams. Examples include: LiveWell (£2.20M; 2010-15; Rochester) a study of interventions for healthy ageing funded by the cross-Research Council Life-Long Health and Wellbeing programme; Limbs Alive (£1.36M; 2012-14; Eyre) a project for monitoring stroke rehabilitation through video gaming funded by the Wellcome Trust-DoH Health Innovation Challenge Fund; and ADD (£641K; 2010-13; Ferrier, Grunze, McAllister-Williams, Watson) an MRC-NIHR EME study on anti-glucocorticoid augmentation of antidepressants. Most recently, we received funding through the Wellcome-EPSRC Innovative Engineering for Health programme (£10M; 2013-20; Ingram, Baker, Cunningham, Trevelyan, Whittaker) to develop an implant for focal epilepsy through to a first-in-man trial. In non-clinical initiatives, Wright had two awards from the multi-agency Insect Pollinators Initiative (£790K; 2011-15) to study nutrition in bees and the impact of environmental toxins on learning. Responding to national priorities, several of our projects directly address issues of assessment and improvement in animal welfare both in laboratory and applied settings, with funding from NC3Rs (£485K; Bateson, Thiele, Rowe) and BBSRC (£680K; Bateson, Smulders).

Responsive Mode Funding: RCUK and Wellcome Trust remain our most important source of funding for studies employing well-defined animal models. Within RCUK our research addresses priority areas for the BBSRC, MRC and EPSRC. Projects funded by the BBSRC have a strong focus on basic neural mechanisms in cognitive processes and systems neuroscience, including: work in NHPs on the neuropharmacology of top-down control (£1.03M; 2008-12; Thiele) and the impact of attention on neuronal adaptation (£576K; 2012-5; Petkov, Vuong); studies on bimanual coordination (£619K; 2008-11; Baker); and studies exploring how cognitive processes are affected by temporal information (£356K; 2010-3; Jennings) or by programming arising from early life adversity (£358K; 2012-6; Bateson, Nettle). Our studies using the NHP model are also funded by the Wellcome Trust, with £2.6M awarded over the REF period for projects on neuronal synchronization in cognition, syntactical learning, auditory processing, and mechanisms of attention (Thiele, Petkov, Rees, Sun, Griffiths). Funding from MRC also supports our NHP work, including the mechanisms of perceptual learning and role of oscillations in cortical networks (£1.53M: 2008-13: Thiele), and is particularly strong in research that underpins medical conditions. Current projects include: examining the inhibitory mechanisms that restrain cortical epileptic activity (£760K: 2012-6; Trevelyan, Racca) and neural mechanisms for movement fractionation in stroke (£689K; 2012-5; Baker). The ESRC supports our work on cognitive processes in humans, such as work on neuropsychological approaches to dissect face perception and perceptual expertise (£312K; 2012-5: **Vuong**). Since 2008 we have expanded our translational programme in neural device development. Awards include an EPSRC Cross-Disciplinary Feasibility Account (Nano-Lab; £202K; Baker, Jackson) which has primed projects on microelectronic engineering with Electrical and Electronic Engineering (UoA13), and an ultra-low power implantable platform for next-generation neural interfaces (£258K; Jackson; with Imperial and Leicester). We received an MRC Milstein Award for innovative research to develop wearable devices for re-programming the nervous system (£407K; Jackson, Baker), and have support to develop a multi-electrode EMG for cross-sectional imaging of muscle (EPSRC; £583K; Whittaker). Aligned with our goal of effective translation we are in



discussion with industrial partners regarding commercialisation of these devices.

Industry and Europe: We have close links with several industrial partners, through directly contracted research (e.g. exploring the effects of 3D viewing (**Read**; <u>BSkyB</u>, UK), examining procognitive properties of novel compounds (**Shoaib**; <u>Johnson & Johnson</u>, USA)), as partners in joint projects (e.g. <u>TSB</u> project with <u>Autifony Therapeutics</u> developing a Kv3-positive modulator for treating schizophrenia (**Cunningham**) and a phase II study of a motilin agonist to improve gastric emptying and motor control in PD with <u>GSK</u> (**Burn**)). As well as receiving industrial grant funding (<u>Codman</u>, <u>Covidien</u>, <u>Microvention</u>, <u>Acandis</u>, <u>Stryker</u>), **White** is a partner in a <u>TSB</u> <u>SMART</u> grant (£250K) with a local SME, <u>IBEX Innovations</u>, to develop novel X-Ray detector technology. Within the EU we currently have <u>FP7</u> funding as part of multi-national consortium to examine a virtual reality-treadmill intervention to reduce falls (V-TIME; value to Newcastle £481K; 2012-15; **Rochester**, **Burn**) and are partners in three vision projects: one funded by the Future Emerging Technology programme to examine encoding in the retina as the basis of novel vision architectures (RENVISION; **Sernagor**), a second based on our work on bio-inspired collision detection (LIVCODE; **Rind**) and a third analysing the effects of LED-based tuneable illumination on visual perception and health (HI-LED; **Hurlbert, McAllister-Williams**).

Charities and Benefactors: We have had funding from a number of disease-focussed charities. Notable current examples are <u>Parkinson's UK</u> support for a longitudinal study of cognitive impairment in PD (ICICLE-PD; £1.2M, 2009-14; **Burn**), and the <u>Michael J Fox Foundation</u> support for comparing clinical scales of cognition in PD (Scale Assessment Study; £771K, 2011-17; **Burn**). General support from benefactors has been an important way of engaging with the wider public, particularly the local community. Notable private donations have been £1M from The <u>Reece Foundation</u> to support our initiative in translational systems neuroscience, the <u>Lockhart Bequest</u> to support research in PD (endowment of £1.05M), and £1M from the <u>Barbour Foundation</u> to support young researchers working on neurodegenerative disease and ageing. This funding has been particularly important in enabling us to provide strategic support for new areas of research.

ii. Infrastructure and Facilities:

Capital Infrastructure: Since 2008 there has been substantial capital investment in our research infrastructure. On the Campus for Ageing and Vitality three new buildings were constructed to support UoA4 research. The Edwardson Building (opened 2008; £7.24M from University and Regional Development Agency) accommodates the Newcastle Brain Tissue Resource (NBTR), advanced neuropathology facilities, a Varian 7T small bore animal MR scanner, and an aged mouse colony. The Clinical Ageing Research Unit (opened 2008; £5.5M Wellcome-Wolfson capital award) is a purpose-built specialist facility for conducting clinical trials in older people which, in addition to generic clinical assessment and one-bedded study rooms, includes laboratories for gait analysis (equipped with Vicon camera system and GaitRite mat) and visual perception studies. The Newcastle Biomedical Research Building (NBRB; £11M funding from NIHR, University and ERDF) provides a translational environment that includes our novel Clinics for Research and Service in Themed Assessment (which combine service excellence for older patients with complex diseases via a multidisciplinary 'one-stop shop' approach with research synergy), bio-gerontology labs for biomarker research, business accommodation for specialist companies in the field of ageing, offices for NIHR-DeNDRoN Coordinating Centre staff, and our Old Age Psychiatry group. These three buildings link with the Henry Wellcome Laboratories for Biogerontology (opened 2003) and Newcastle Magnetic Resonance Centre (opened 2006) to create a world class research campus with high quality facilities for imaging, biomarker research, biobanking and early phase clinical trials, with a key focus around neurodegeneration and ageing. The Campus also includes the Wolfson Research Building which was refurbished in 2012 to provide high quality accommodation for our research in Affective Disorders, with adjacencies to an inpatient unit for the Regional Affective Disorders Service (opened 2010) and EEG labs located in the NBRB.

Our programmes in early diagnostic markers for LBD and in novel markers for affective disorders are a core element of the University-wide initiative to enhance PET imaging capabilities. Following the installation in 2007 of a clinical PET-CT scanner (Siemens Biograph-40) at the Newcastle MR Centre, during the REF period we installed a Philips Mosaic HP animal PET-CT facility (£500K; operational in 2009), and in 2012 a PET Tracer Production Unit was opened in the School of Chemistry to capitalise on our expertise in the synthesis of 18F-labelled tracers. This £1.13M investment (funding by the Regional Development Agency and <u>Sir Bobby Robson Foundation</u>) includes an Advanced Biomarker Technology ultra-compact cyclotron, only the second of its type



in the world. On the Medical School campus a major new development supports our internationally renowned NHP and systems neuroscience programmes. Investment by the <u>Wellcome Trust</u> and University (£13.5M) funded new NHP housing and laboratory facilities, and an extension to our main neuroscience building to create the Centre for Translational Systems Neuroscience (opened 2013). This provides new capabilities, including high density EEG and image-guided Transcranial Magnetic Stimulation, which will contribute to our future translational programmes. These new facilities are adjacent to our Bruker 4.7T vertical bore MR scanner dedicated for NHP imaging which was upgraded in 2012 to multi-channel imaging through a <u>Wellcome Trust</u> equipment grant (£373K). Our work on comparative behaviour has benefitted from the installation of three climate controlled chambers to replicate natural conditions in a controlled environment (<u>BBSRC</u>, £136K).

e. Collaboration or contribution to the discipline or research base

i Collaboration:

UoA4 investigators collaborate widely, as evidenced by the fact that 65% of submitted outputs include external collaborators. Of note are the national and international networks we have established to enable our large scale clinical trials work. Examples include, the international consortium of 78 recruiting centres that underpins our neurosurgical trials of intracranial haemorrhage (STICH/STITCH-Trauma; Lancet), and the network of centres delivering of robot assisted therapy or enhanced therapy in our rehabilitation trials (RATULS / EXTRAS). The ability to apply complementary approaches through collaboration has led to high profile outputs from our work on the identification of neuronal activity within regions of the macague cortex selective for communication signals (Current Biol, Nat Neurosci; Petkov with Tübingen) and work demonstrating the effects of chemical modulators of honey-bee behaviour (Science, Nat Commun; Wright with Royal Botanical Gardens and Dundee). Notable examples of international collaborations have included our work on neural coding in the primate visual system (PNAS, J Neurosci; Thiele with Barcelona, Salk Institute, and Amsterdam), and the analysis of cortical activity in epileptic patients that has revealed hypersynchronous activity in the seizure focus and patterns of propagation (Nat Commun. Brain; **Trevelyan** with Columbia). Many of these collaborations are funded via joint RCUK support, the EU or co-funding with national agencies. Some of our researchers hold recognised positions at collaborating institutions enabling them to manage research staff. For example, Griffiths is Honorary Professor at the Wellcome Trust Centre for NeuroImaging, and Adjunct Professor in Neurosurgery at Iowa University where he employs researchers to conduct intraoperative recordings from human auditory cortex (Current Biol, J Cogn Neurosci). In recognition of his collaboration on reproductive psychology (PLoS One; Proc Roy Soc B) Nettle was appointed a Royal Netherlands Academy of Arts and Sciences visiting professor at Groningen. In addition to individual collaborations, over the REF period we have developed a strategic partnership with Monash University, and links with centres in countries with emerging scientific programmes in neuroscience, including the Institute of Neurosciences, Kolkata, India (on devices for diagnosis and interventions in neurology) and the Institute of Primate Research, Nairobi, Kenya (on models of neurovascular disease and stroke, and characterisation of the primate motor system). These support training opportunities for both partners and access to unique research resources.

We host numerous administrative structures and research resources that facilitate collaboration at national and international levels. We have hosted three NIHR Topic-Specific Research Networks which have major roles in delivering clinical research nationally: the Dementia and Neurodegenerative Diseases Research Network (DeNDRoN; Director: McKeith; Associate Director: Burn), the Stroke Research Network (Director: Ford; Deputy Director: Rodgers) and the North East Hub of the Mental Health Research Network (Lead: Ferrier). A number of projects have arisen directly from the activity of these networks and the three themes will continue in the transition to a Local Clinical Research Network in 2014. We are also the lead Institution for a number of resources which support both our research and wider collaboration. Notably, the NBTR has an outstanding collection of post-mortem brain tissue from clinically well-characterised cases of dementia and other neuropsychiatric and neurodegenerative disorders, and is part of the UK CRC Brain Bank Strategy, funded by the MRC to support research into neurological disease. MRC have provided support through two awards in the REF period (total £730K; Attems, Kalaria, Morris, Polvikoski, **Thomas**) and a renewal until 2018 (£1.2M). We are a member of the Brains for Dementia network, which recently received renewed funding from Alzheimer's Brain Bank UK (£480K, 2013-18). In affective disorders research we have generated a well-characterised cohort of bipolar-II patients through the MRC-NIHR Patient Research Cohorts Initiative (£687K; 2009-14; Ferrier, Grunze) that



supports collaboration on phenotype characterisation and genetic markers of bipolar disorder. Responding to the government and funding agencies' priority to increase data sharing, we are the lead for the CARMEN neurophysiology data sharing initiative which was established through EPSRC e-science programme to fund a consortium of 11 UK universities (£4.3M; 2006-11; PI: **Ingram** plus **Baker, Sernagor** at Newcastle) and is currently supported by the BBSRC Biotechnology and Biomedical Resources Fund (£906K; 2010-14; joint with York).

In translating clinical research into practice, UoA4 investigators have had major roles in developing evidence-based guidelines. **McKeith** advised the DSM-5 Task Force on neurocognitive disorders which accepted LBD into the new diagnostic system. **Burn** is a member of international consortia proposing diagnostic criteria for dementia and mild cognitive impairment in people with PD. **Grunze** is Secretary to the World Federation of Societies of Biological Psychiatry Task Force on Treatment Guidelines for Bipolar Disorders. **McAllister-Williams** and **Ferrier** co-authored the British Association for Psychopharmacology antidepressant guidelines. **Rodgers** and **White** are on the Inter-collegiate Stroke Working Party which oversees National Stroke Audit and National Clinical Guidelines for Stroke.

ii Contribution to the Research Base: Our investigators have made many important contributions to shaping and influencing the national and international research base in their specific fields. We have returned two Fellows of the Academy of Medical Sciences (Griffiths, McKeith) and five NIHR Senior Investigators (Burn, Ferrier, Ford, McKeith, Rodgers), and in 2013 Ford was appointed CBE for services to research in stroke medicine. The returned UoA4 investigators are represented on the editorial boards of 37 journals, including Current Biol, Brit J Psychiat and Proc Roy Soc B. We contribute to the national and international peer review process for funding through key involvement on grant panels. As examples: Bateson serves on BBSRC Committee A (Deputy Chair since 2012); Thiele sits on the MRC Neurosciences and Mental Health Board and served on BBSRC Committee A; Ferrier and Griffiths served on the Wellcome Trust Neurosciences and Mental Health panel; Rodgers is on the NIHR HTA Clinical Evaluation and Trials Board; Ford is on the NIHR Strategy Board; and Burn is on the MRC EME Prioritisation Group. McKeith influences key changes in strategic delivery of NIHR portfolio trial activity through his role in the NIHR Clinical Research Network Transition Board. In the area of training: Rowe is on the BBSRC Training Awards Committee: Kalaria is on the MRC Clinical Fellowship Board: McAllister-Williams is on the MRC Clinical Training and Career Development Panel; and Baker is on the NC3Rs David Sainsbury Fellowships Award Panel. Internationally: Kalaria was Chair (Science Review Panel) for the Fogarty-NIH Brain Disorders across Lifespan programme and Racca is a Committee member for FP7-People-ITN EU LIF. We contribute to the strategic direction and funding provided by many charitable organisations that support research, including Alzheimer's Society Project Grant Panel (Morris); Alzheimer's Research UK Scientific Advisory Board (Kalaria); Parkinson's UK Research Advisory Panel (Rochester, Burn); Action on Hearing Loss Grants Panel (Rees); Stroke Association Scientific Committee (Rodgers, White); and Multiple System Atrophy Trust Scientific Advisory Panel (Chair: Burn). Bruce is a Vice-President of the British Academy and Read served on the Royal Society Strategic and Operational Review Steering Group. We conduct a wide range of formal and informal advisory work for external organisations which allows us to benchmark our science and to identify research priorities. As examples: **Hurlbert** is on the visiting group for Brain and Cognitive Sciences at MIT and is Scientific Trustee of the National Gallery; Thiele is on the Advisory Board for the Werner-Reichardt-Centrum, Tübingen; and Rind is a Technical Advisor to the Defence Scientific Advisory Council. Over the REF period UoA4 investigators have contributed widely to the activities of professional societies including: **McKeith** (President, Lewy Body Society); Ford (Board of Directors, European Stroke Organisation); Mendelow (Vice-Chair, World Federation of Neurosurgical Societies Neurotrauma Committee); Kalaria (Secretary-General, International Society of Vascular Behavioural and Cognitive Disorders); Ferrier (President) and McAllister-Williams (General Secretary: British Society for Psychopharmacology): Ingram (Secretary, British Neuroscience Association); and Nettle (President, European Human Behaviour and Evolution Association). Members of CBE have key involvement with the Association for the Study of Animal Behaviour (ASAB): Rowe is Secretary and the CBE hosted the first joint meeting of ASAB and the International Ethological Conference Behaviour 2013 which attracted 900 delegates. Kalaria and Sernagor have made notable contributions to supporting neuroscience in developing countries through their involvement in the International Brain Research Organisation Schools Programme.