

UCT Neurology Research Group

Neurological Diseases Research Fund



Neurological Diseases Research Fund

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Overview

The Neurology Unit of the University of Cape Town (UCT) is a dynamic teaching and research facility for the neurosciences. It falls under the UCT Faculty of Health Sciences which, in 2012, became the first tertiary institution in Africa to be placed in the Top 50 health universities in the world for pre-clinical, clinical and post-graduate training.

The UCT Faculty of Health Sciences has built a reputation for the excellence of its teaching, training and cutting edge research; and its graduates and postgraduates are highly regarded internationally. Moreover, the Faculty publishes more peer reviewed papers in high impact journals than any other health faculty in the country. It has kept pace with global trends and evidence-based approaches to Academic Health Sciences and, in so doing, it has contributed significantly to the overall improvement of the health status of sub-Saharan Africans as well as contributing very materially to building clinical neuroscience research capacity relevant to our continent.

More than a decade ago, the **Neurology Research Group** was established within the Division of Neurology at the University of Cape Town with the specific aim of further promoting research into neurological disorders prevalent in sub-Saharan Africa including but not confined to stroke, dementia, neuropathy, and Myasthenia Gravis, as well as HIV- and tuberculosis-related neurological illnesses. Members of the Group have conducted research and closely supervised

postgraduate students working towards their Master's degrees or doctorates in the fields of clinical neuroscience or related molecular and cell biology. These students have performed extremely well, many obtaining their postgraduate degrees with distinction. At the same time these students and other members of the Group have produced important clinically meaningful research while publishing numerous peer-reviewed articles in international journals.

The Neurology Research Group receives very little in the way of monetary or financial contributions from the University of Cape Town. Instead, it is dependent on research grants from local and international research bodies. Moreover, most of the Group's post-graduate students are at the beginning of their careers and, consequently, they do not have an established curriculum vitae with sufficient publications to attract adequate funding for their research projects. With this in mind, the **Neurological Diseases Research Fund (NDRF)** has been established with the specific aim of facilitating "start-up" funding for such students when they begin their projects or "top-up" funding, when this is required during the course of their research.

Donations to the UCT Neurological Diseases Research Fund

The Neurology Research Group invites donations to the UCT Neurological Diseases Research Fund. These will enable the Group to continue its important established research programmes and support capable young post-graduate fellows as they complete their Masters and PhD degrees in an environment in which it is very difficult to attract funding for their research. We welcome all donations to the fund. Should donors wish to make a bequest and ear-mark the donation for a specific neurological disorder or programme listed within the groups' current areas of expertise, then such monies will be allocated accordingly. Donors will also be provided with feedback on the progress of the research projects they support. [Email: alan.bryer@uct.ac.za](mailto:alan.bryer@uct.ac.za)

Members of the UCT Neurology Research Group

Director:	Associate Professor Jeannine Heckmann
Head of Neurology:	Associate Professor Alan Bryer
Head of Geriatric Medicine:	Prof Marc Combrinck
Neurologists:	Dr Kathleen Bateman
	Dr Lawrence Tucker
	Dr Edward Lee Pan
	Dr Suzaan Marais (affiliated)



Research areas

Stroke

Stroke is estimated to be the most common cause of permanent neurological disability and a common cause of death in Southern Africa. Clinical and laboratory-based research projects run by the Group are focusing on causes of stroke in young persons; in addition a longitudinal study is under way to evaluate the underlying biological mechanisms in HIV-associated stroke. The Group was also instrumental in drawing up the current national stroke treatment guidelines and set up what still remains the only dedicated Stroke Unit in the South African Public Health Sector.

Dementia

Clinical and laboratory-based research has been undertaken and is ongoing into neurodegenerative conditions causing dementia in the Southern African context including Alzheimer's disease and the neurocognitive disorders associated with HIV.

Neuromuscular disorders and neuroimmunology

The Neurology Group runs the largest and most dynamic Myasthenia Gravis Research Unit on the African Continent, as well as providing quaternary level care for patients with this condition referred from both the public and private health care sectors. Ongoing clinical and laboratory-based research projects are focussing on improving therapeutic strategies and increasing understanding of complications of this disease relevant to Africa. In collaboration with the University of Stellenbosch, the Group has recently started research on Motor Neuron Disease and runs a dedicated specialist patient clinic caring for patients with this condition. Projects related to neuromuscular disease in HIV-infected subjects focusing on the impact of aging are ongoing. Moreover, the Neurology Group is co-ordinating the South African research participation in the International Guillain-Barre Syndrome (GBS) Outcome Study, a multicentre study looking at biomarkers that predict outcome in GBS.



Neurological Infectious Diseases

The Group has established clinical and laboratory-based research projects to investigate the risk factors associated with the development of neuropathy in HIV-infected subjects and the work performed thus far has produced important insights and numerous publications. The incidence of tuberculosis (TB) in Southern Africa, and Cape Town in particular, is amongst the highest in the world. Important research has been started by the Group assessing the impact of TB meningitis on the cognitive morbidity in adults. Research efforts in bacterial meningitis have looked at promoting early, accurate diagnosis of meningitis, including reporting unusual presentations of this disease.

Neurogenetics

Long-standing clinical and laboratory-based research has been established for patients with inherited neurodegenerative conditions such as familial spinocerebellar ataxia (SCA). Current research is directed at developing an alternative multiplex PCR technique for the molecular diagnosis of the most common SCAs. Molecular studies are planned in order to reveal potential founder effects within the Southern African region.

Epilepsy

There are approximately 2 specialist neurologists and 1 neuro-technologists practicing per million population in South Africa and significantly fewer in our neighbouring states. We are committed to the training of competent healthcare professionals in the neurological sciences and, to this end, the Group is setting up a geographically efficient web-based distance-learning platform for neurophysiology training in electroencephalography (EEG). Other clinically relevant courses will follow. The project has the support of the World Federation of Neurology, the International League Against Epilepsy and the Neurological Association of South Africa. It is anticipated that the majority of sub-Saharan career neurology registrars and many neuro-technologists will enrol and the programme will be tested for efficacy.

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Photo by Danie van der Merwe

Addendum:**Peer reviewed papers emanating from the UCT Neurology Research Group (2009-2015):****International publications:**

Limb-girdle weakness in a marfanoid man: distinguishing calpainopathy from Becker's muscular dystrophy. G Shaboodien, DA Watkins, K Pillay, P Beighton, JM Heckmann, BM Mayosi. *Pract Neurol* 2015;0:1–3.

High levels of von Willebrand factor and low levels of its cleaving protease, ADAMTS13, are associated with stroke in young HIV-infected patients. S Allie, A Stanley, A Bryer, M Meiring, MI Combrinck. *Int J Stroke*. 2015 Jun 29. doi: 10.1111/ijis.12550. [Epub ahead of print]

Incidence of acetylcholine receptor-antibody-positive myasthenia gravis in South Africa. B Mombaur, MR Lesosky, L Liebenberg, H Vreede, JM Heckmann. *Muscle Nerve* 51: 533–537, 2015

Magnetic Resonance Imaging of the Spine in HIV-associated Tuberculous Meningitis Immune Reconstitution Syndrome Presenting as Myeloradiculopathy. Kathleen Bateman. *International Journal of Clinical & Medical Imaging* 2014; 1(2). *Clinical Image*. doi: 10.4172/ijcmi.1000138

Impact of living and socioeconomic characteristics on cardiovascular risk in ischemic stroke patients. Amarencu P, Abboud H, Labreuche J, Arauz A, Bryer A, Lavados PM, Massaro A, Munoz Collazos M, Steg PG, Yamout BI, Vicaut E; OPTIC Registry Investigators. *International Journal of Stroke*. 2014 Jun 12. doi: 10.1111/ijis.12290. [Epub ahead of print].

The effects of prednisone and steroid-sparing agents on Decay Accelerating Factor (CD55) expression: implications for Myasthenia gravis. Auret J, Abrahams A, Prince S, Heckmann JM. *Neuromuscular Disorders* 2014; 24:499-508

Sensory polyneuropathy in human immunodeficiency virus-infected patients receiving tuberculosis treatment. Centner C, Carrara H, Benatar M, Harrison TB, Heckmann JM. *International Journal of Tuberculosis and lung diseases* 2014; 18(1):27-33

Plasma cytokine profiles in HIV-1 infected patients developing neuropathic symptoms shortly after commencing antiretroviral therapy: a case control study. JJ van der Watt, K Wilkinson, R Wilkinson, JM Heckmann. *BMC Infectious diseases* 2014; 14:71

Incidence of acetylcholine receptor positive Myasthenia Gravis in South Africa. Mombaur B, Lesosky L, Liebenberg L, Vreede H, Heckmann JM. *Muscle & Nerve* 2014 Doi:10.1002/mns.24348 [epub ahead of print].

Thrombolysis for acute ischaemic stroke in South Africa. Bryer A. Wasserman S. *International Journal of Stroke* 2013 Suppl A100:112-3. Doi: 10.1111/ijis. 12059. Epub 2013 May22

Mitochondrial genomics and antiretroviral therapy-associated metabolic complications in Black South Africans: a pilot study. Sinxadi P, Dave JA, Samuels DC, Heckmann JM, et al. *Aids Research and Human Retroviruses* 2013; 29 DOI: 10.1089/aid.2012.0373.

Manifestations of HIV infection in the peripheral nervous system. Centner CM, Bateman KJ, Heckmann JM. *Lancet Neurology* 2013; 12: 295-309.

Molecular characterisation of brain virus in patients with measles inclusion body encephalitis (MIBE). Hardie DR, Albertyn C, Heckmann JM, Smuts HEM. *Virology Journal* 2013; 10:283

Reliability and diagnostic performance of CT imaging criteria in the diagnosis of tuberculous meningitis. Botha H, Ackerman C, Candy S, Carr JA, Griffith-Richards S, Bateman KJ. *PLoS One*. 2012;7(6):e38982. doi: 10.1371/journal.pone.0038982. Epub 2012 Jun 29. PMID: 22768055

Relationship between apolipoprotein E4 genotype and white matter integrity in HIV-positive young adults in South Africa. Hoare J, Westgarth-Taylor J, Fouche J-P, Combrinck M, Spottiswoode B, Stein DJ, Joska JA. *Africa. European Archives of Psychiatry and Clinical Neuroscience* 2012; 263: 189-195.

HIV infection and stroke: current perspectives and future directions. Laura A Benjamin, Alan Bryer, Hedley CA Emsley, Saye Khoo, Tom Solomon, Myles D Connor. *Lancet Neurology* 2012; 11(10) 878-890.

Demographics, socio-economic characteristics, and risk factor prevalence in patients with non-cardioembolic ischaemic stroke in low- and middle-income countries: the OPTIC registry. Abboud H, Labreuche J, Arauz A, Bryer A, Lavados PG, Massaro A, Munoz Collazos M, Steg PG, Yamout BI, Vicaut E, Amarenco P; for the OPTIC Registry Investigators. *International Journal of Stroke*. 2012 Sep 13. doi: 10.1111/j.1747-4949.2012.00893.x. [Epub ahead of print]

White Matter Damage in Clade C HIV-Positive Subjects: A Diffusion Tensor Imaging Study. Hoare J, Fouche J-P, Spottiswoode B, Sorsdahl, K, Combrinck M, Stein DJ, Paul RH, Joska JH. *Journal of Neuropsychiatry and Clinical Neurosciences* 2011; 23 (3): 308-315.

The South African guideline for management of ischaemic stroke and transient ischaemic attack: recommendations for a resource constrained health care setting. A Bryer, MD Connor, P Haug, B Cheyip, H Staub, B Tipping, W Duim, V Pinkney-Atkinson. *International Journal of Stroke* 2011;6(4): 349-354.

The great pretender. S Wasserman, Y Vallie, A Bryer. *Lancet* 2011;377:1976

Polyneuropathy, Anti-Tuberculous Drug Therapy and the Role of Pyridoxine in the HIV/AIDS era: A Systematic Review. Van der Watt J, Harrison T, Benatar M, Heckmann JM. *International Journal of Tuberculosis and lung diseases* 2011; 15 (6):722-728.

Characterization of HIV-Associated Neurocognitive Disorders Among Individuals Starting Antiretroviral Therapy in South Africa. Combrinck M, Paul RH, Stein DJ, Flisher AJ. *AIDS and Behavior* 2011; 15(6): 1197-1203.

A single blinded trial of methotrexate versus azathioprine as steroid-sparing agents in newly diagnosed myasthenia gravis. Heckmann JM, Rawoot A, Bateman K, et al. *BMC Neurology* 2011; 11:97

Stroke: working toward a prioritized world agenda. Hachinski V, Donnan GA, Gorelick PB, Hacke W, Cramer SC, Kaste M, Fisher M, Brainin M, Buchan AM, Lo EH, Skolnick BE, Furie KL, Hankey GJ, Kivipelto M, Morris J, Rothwell PM, Sacco RL, Smith SC Jr, Wang Y, Bryer A, Ford GA, Ladekola C, Martins SC, Saver J, Skvortsova V, Bayley M, Bednar MM, Duncan P, Enney L, Finklestein S, Jones TA, Kalra L, Kleim J, Nitkin R, Teasell R, Weiller C, Desai B, Goldberg MP, Heiss WD, Saarela O, Schwamm LH, Shinohara Y, Trivedi B, Wahlgren N, Wong LK, Hakim A, Norrving B, Prudhomme S, Bornstein NM, Davis SM, Goldstein LB, Leys D, Tuomilehto J. *Stroke*. 2010 Jun;41(6):1084-99. Also in: *Cerebrovascular Diseases*. 2010 May 24;30(2):127-147.

Polymyositis in African HIV-infected subjects. Heckmann JM, Pillay K, Hearn AP, Kenyon C. *Neuromuscular Disorders* 2010; doi:10.1016/j.nmd.2010.06.007

HIV- neuropathy in South Africans. Frequency, characteristics and risk factors. Maritz J, Benatar M, Dave J, Harrison T, Badri M, Levitt N, Heckmann JM. *Muscle & Nerve* 2010; 41: May 599-606.

Association between Apolipoprotein E genotype and human immuno-deficiency virus-associated dementia in younger adults starting antiretroviral therapy in South Africa. Joska J, Combrinck M, Valcour V, Hoare J, Leisegang F, Mahne AC, Myer L, Stein DJ. *Journal of Neurovirology* 2010; 16(5): 377-383.

A functional SNP in the Regulatory region of the Decay Accelerating Factor gene associates with extraocular muscle pareses in Myasthenia Gravis. Heckmann JM, Uwimpuhwe H, Ballo R, Kaur M, Bajic VB, Prince S. *Genes & Immunity* 2010; 11: 1-10.

Stroke care in a rural African setting. S Wasserman, L de Villiers, A Bryer. *International Journal of Stroke* 2009;4 (3):151

Opsoclonus myoclonus syndrome in HIV. Scott K, Parker F, Heckmann JM. *Journal of Neurological Sciences* 2009 doi:10.1016/j.jns.2009.04.026

Olfactory impairment is more marked in patients with mild dementia with Lewy bodies than those with mild Alzheimer's disease. Williams SS, Williams J, Combrinck M, Christie S, Smith AD, McShane R. *Journal of Neurology, Neurosurgery and Psychiatry* 2009; 80: 667-670.

Local publications:

Encephalopathy after persistent vomiting: Three cases of non-alcohol-related Wernicke's encephalopathy. K Antel, N Singh, B Chisholm, JM Heckmann, S Afr Med J 2015;105(6):442-443

Thrombolysis risk prediction: applying the SITS-SICH and SEDAN scores in South African patients. A von Klemperer, K Bateman, J Owen, A Bryer. Cardiovasc J Afr. 2014 Sep-Oct;25(5):224-7.

Acute intermittent porphyria presenting as progressive muscular atrophy in a young black man. CH Albertyn, M Sonderup, A Bryer, A Corrigan, P Meissner, JM Heckmann. S Afr Med J. 2014 Apr;104(4):283-5.

Listerial Brainstem Encephalitis – treatable, but easily missed. P Fredericks, M Britz, R Eastman, JA Carr, KJ Bateman. S Afr Med J, January 2015.

Neuropsychiatric symptoms in patients with thymoma-associated and non-thymoma myasthenia gravis. Freeman CF, Lewis I, Heckmann JM. South African Journal of Psychiatry 2014; 20;2:50-53

Acute intermittent porphyria presenting as progressive muscular atrophy in a young black man. Albertyn CH, Sonderup M, Bryer A, Corrigan A, Meissner P, Heckmann JM. S Afr Med J 2014; 104: 283-285.

Recommendations for the use of immunoglobulin therapy for immunomodulation and antibody replacement: CME article. Peter JG, Heckmann JM, Novitsky N. S Afr Med J 2014; 104: 11; 796

HIV-associated neurocognitive disorders: antiretroviral regimen, central nervous system penetration effectiveness, and cognitive outcomes. Cross HM, Combrinck MI, Joska JA. S Afr Med J 2013;103:758-762

Guidelines for the management of acute meningitis in children and adults in South Africa. T Boyles, C Bamford, K Bateman, L Blumberg, A Dramowski, A Karstaedt, S Korsman, D le Roux, G Maartens, S Madhi, R Naidoo, Ja Nuttall, G Reubenson, J Taljaard, J Thomas, G van Zyl, A von Gottberg, A Whitelaw, M Mendelson. FIDSSA Working Group on Acute Meningitis in Children and Adults. Southern African Journal of Epidemiology and Infection 2013;28(1):5-15

Stroke Management and the new antithrombotic drugs - a revolution in stroke management. A Bryer. Cardiovascular Journal of Africa. S Afr Med J 2012;102(6):541-544.

Inherited polyglutamine spinocerebellar ataxias in South Africa. DC Smith, A Bryer, LM Watson, J Greenberg. S Afr Med J 2012;102 (8); 683-686.

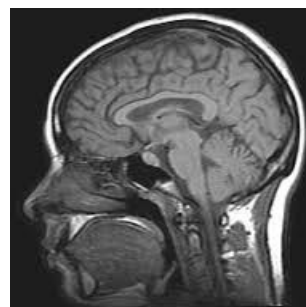
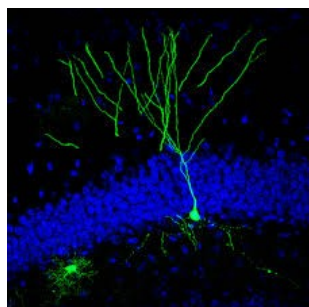
Early outcomes of thrombolysis for acute ischaemic stroke in a South African tertiary care centre. S Wasserman, A Bryer. South African Journal of Medicine. S Afr Med J 2012;102(6):541-544.

Stroke outcomes in a socio-economically disadvantaged urban community. L De Villiers, M Badri, M Ferreira, A Bryer. S Afr Med J 2011;101:345-348

Silent casualties from the measles outbreak in South Africa. Albertyn C, van der Plas H, Hardie D, Candy S, Moroka T, LeePan EB, Heckmann JM. S Afr Med J 2011; 101(5):313-317.

South African guideline for management of ischaemic stroke and transient ischaemic attack 2010: A guideline from the South African Stroke Society (SASS) and the SASS Writing Committee. A Bryer, MD Connor, P Haug, B Cheyip, H Staub, B Tipping, W Duim, V Pinkney-Atkinson. S Afr Med J 2010;100(11) part2:747-778

The need for a community-based model for stroke care in South Africa. Bryer A. S Afr Med J 2009;99(8):574-575. Community-based care of stroke patients in a rural African setting. S Wasserman, L de Villiers, A Bryer. S Afr Med J 2009;99 (8):579-583.



Degrees achieved by fellows supervised by the UCT Neurology Research Group (2009-2015):

Post-doctoral fellows:

Post doctorate 2010-2012: The effects of prednisone and steroid-sparing agents on Decay Accelerating Factor (CD55) expression: implications for Myasthenia gravis. Abrahams A

PhD degrees:

PhD (Medicine) 2013: HIV-associated sensory neuropathy in an African cohort: a longitudinal study of risk factors predisposing to antiretroviral induced painful neuropathy. Van der watt JJ

PhD 2013: Relationships between psychosocial stress, cortisol, apolipoprotein E4, beta amyloid, hippocampal volume and Alzheimer's disease in a sample of South African older adults. James KA

PhD 2013: The relationships between Alzheimer's disease, inflammation, the APO E genotype and neuronal integrity. Grace L

MSc degrees:

MSc (Medicine) 2015 (Distinction) : Distal sensory polyneuropathy and associated risk factors in community-based South Africans with HIV after twelve months of anti-retroviral therapy. Vermaak J-R.

MMed (Neurology) 2015: The utility of CSF PCR in central nervous system Varicella zoster infection in HIV. Stanley A.

MSc (Med) 2014. The associations between plasma homocysteine, vitamin B12, folate, the apolipoprotein E genotype and Alzheimer's disease. Mohamed I.

MSc (Med) (with distinction) 2014: The role of systemic inflammation and the apolipoprotein E gene in human immunodeficiency virus-associated cognitive impairment. van Brakel E.

MMed (Neurol) (with distinction) 2014: A review of cases of motor neurone disease seen at Groote Schuur Hospital from 2005 to 2010. Daude A.

MMed (Neurology) – submitted 2014: Subacute measles encephalitis: the neurological sequelae of the measles outbreak in South Africa. Albertyn C.

BSc Hons (Cell Biol) course work and mini dissertation: Studying the functionality of African-specific variations of the Transforming Growth Factor B1 regulatory region. Buys J-M.

MSc (Medicine) 2013 (Distinction): the role of von Willebrand factor and its cleaving protease, ADAMTS13, in young patients with HIV-related stroke. Sallie S.

MSc (Cell Biology) 2013: Identifying the molecular basis for treatment resistance in a subset of Myasthenia gravis patients of African ancestry. Auret J.

MSc (Med) (with distinction) 2012: HIV-associated neurocognitive disorders: biomarkers and the response to anti-retroviral therapy. Cross H.

MSc (Medicine) 2012: Distal sensory polyneuropathy in HIV/TB co-infection: the role of Vitamin B6 status and NAT 2 genetic variation. Centner C.

MMed (Psychiatry) 2012: Neuropsychiatric symptoms in patients with thymoma-associated and non-thymoma myasthenia gravis. Freeman CF.

MMed (Neurology) 2012 (Distinction). Early outcomes of thrombolysis for acute ischaemic stroke in a South African Tertiary Centre. Wasserman S.

MSc (Medicine) 2011: Identification of a suitable SNP for allele-specific silencing of the disease causing gene in

SCA1 patients in South Africa. Baine FK.

MSocSci 2010: The relationship between stress, inflammation and Alzheimer's disease. Grace L.

MSc (Med) 2010: The role of inflammation, oxidative stress and the apolipoprotein E genotype in HIV-associated cognitive impairment: a clinical, biochemical and neuro-imaging study. Mahne AC.

MMed (Family Med) 2010: The morbidity associated with painful neuropathy in HIV-infected subjects on antiretroviral therapies: An assessment of self management strategies. Ismail M.

MSc (Medicine) 2009 (Distinction): Distal sensory polyneuropathy in South African infected with HIV: a cross-sectional analysis of a community based cohort. Maritz J.

MSc (Cell Biol) 2009 (Distinction): Molecular analysis of Decay Accelerating Factor as a potential susceptibility factor to developing treatment resistant extraocular muscle involvement in Myasthenia Gravis. Uwimpuhwe H.

Current students:

A/Prof Heckmann (supervisor)	Dr M Nel—PhD Dr R Rautenbach—MSc Dr A Waweru—MMed Ms J-M Buys—MSc M Borkum—PhD H Bagula —MPH B Mombaur —MPH
Dr Bateman (supervisor)	Dr C Albertyn—MSc
A/Prof Bryer (supervisor)	Dr D Smith—Post doctoral fellow Dr W Matshikiza—MMed Dr. I Ebrahim-MMed Dr. V. Vimbai Mandizvidza -MPH
Prof Combrinck (supervisor)	Mr B Christ—PhD Dr MV Gule—MMed Dr H Jeena—MSc (Med) Dr Lina Groenewald MPhil (Psychiatry)

Students from international universities who have published under the NRG:

K Scott, University College London, UK; 2009
A Hearne, University College London, UK; 2010
N Faunce (in preparation), University of Kansas, USA; 2014