Kingdom of Saudi Arabia
Ministry of Higher Education
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المملكة العربية السعودية
وزارة التعليم العالي
الملحقية الثقافية
بالمملكة المتحدة وايرلندا

DIVISION OF HIGHER EDUCATION

SEMI-ANNUAL EVALUATION REPORT FOR SAUDI STUDENTS DOING THEIR DEGREES BY RESEARCH

Period covered by this report :from to

Section 1- GENERAL INFORMATION:

1. **Students Name:** SUFANA AL-MASHADI 2. **Our Reference Number:**
3. **Your Reference Number:**
4. **Course Details:**
   A. Name of Institution: SHEFFIELD UNIVERSITY
   B. Department: SHEFFIELD INSTITUTE FOR TRANSLATIONAL NEUROSCIENCE
   C. Degree Registered for: MPhil (PhD) Other
   D. Duration of the Program: 3 Years
   E. Major Field of Study: NEURODEGENERATION
   F. Specific Field of Study: CELLULAR INJURY IN WHITE MATTER.
   G. Date of First Registration: 10-1-11
   H. Expected Date of Completion/Submission: 4-1-14
   I. Expected Date of Viva: NOT YET PLANNED.

Section 2- RESEARCH DETAILS: OXIDATIVE STRESS AND DNA DAMAGE IN
(a) Thesis Proposal Title: WHITE MATTER LESIONS OF THE AGEING HUMAN BRAIN
(b) Current Stage of Study: 1st year 2nd year (3rd year).

Current stage of study	Yes	No	N/A*
Review of literature	✓		
Design of experiment(s)	✓		
Data collection/Experimental work	✓		
Data analysis and interpretation	✓		
Writing up and revising the thesis for submission			✓

*N/A= Not Applicable

Section 3- ACADEMIC CONTRIBUTIONS:

Since the starting date of the student, which accomplishments have been achieved in the following areas? (Use attachments, if necessary)

National/ Regional Conferences Attended:

BRITISH NEUROPATHOLOGICAL SOCIETY, MARCH 2013

BRITISH NEUROSCIENCE ASSOCIATION, APRIL 2013.

Papers Published:

- NONE.
- EARLY DRAFT IN PREPARATION

Posters Given:

- AT BOTH MEETINGS ABOVE. (PHOTOCOPY OF PUBLISHED ABSTRACT FROM BNS + BNA ATTACHED).

Rewards/Awards:

Section 4- ACADEMIC PERFROMANCE:

(a) Frequent consultation with supervisor during period of this report:

Seldom Sometimes Often Very Often

(b) Please complete the table on page three by using this rating scale ranging from 1 – 5, with 1 being the least satisfactory and 5 being the most satisfactory.

RATING SCALE

5: Outstanding: Exceeds expectation - A truly **outstanding** student in all respects within a given category.

4: *Very Good*: *Meets expectation* - An **above average** student who frequently demonstrates above average performance.

3: Good: *Meets expectation* - An **average** student with "middle of the road" approach with potential to improve with time.

2: *Borderline*: *Marginal* - **Below average** student who has deficiencies.

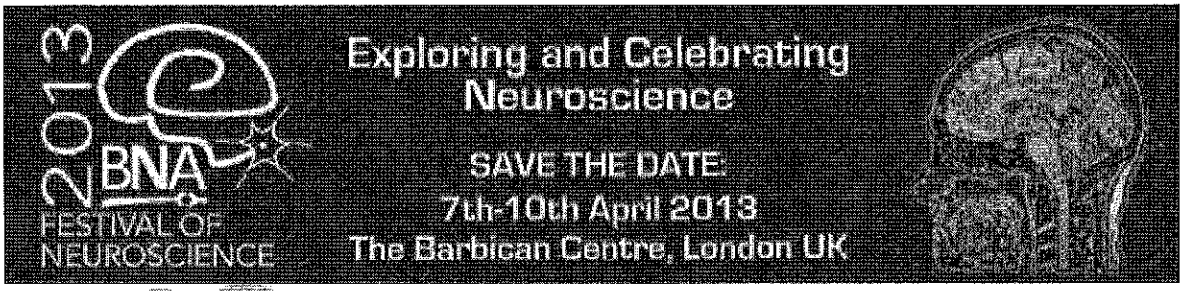
1: Unsatisfactory: ***Does not meet expectation*** - student who has **gross deficiencies** in a major area of studying.

Statement	Rating*
RESEARCH PROGRESS	
Student's research progress in regards of meeting the goals and time-line: Please comment: Proceeding well. Has generated good data and is now moving into a final phase of the study.	5
PROFESSIONAL ATTITUDES AND BEHAVIORS	
Interpersonal relations/teamwork (effectiveness in working with peers and supervisors)	5
Commitment (Dedicated in pursuing studies)	5
Ability to work independently	5
Accepts constructive criticism and knows own limitations	5
Language proficiency	5
Knowledge Base and Practical Skills in Specialty	
Grasp of knowledge In the field of study	5
Knowledge of research methodology including critical appraisal of scientific literature.	5
Critical review of Literature	5
Ability to make effective public presentations of research results	5
Quality of records/reports	5
Ability to interpret & present results	5
Principals of ethics & originality	5

*If the criteria not applicable please write n/a

(c) Please use the attached separate sheet for additional comments, and points of strength/weakness, if any, and whether they have been pointed to the student.

This form was filled by: Dr. S. WHARTON
Position: READER IN NEUROANTHROPOLOGY
Telephone Number: +44 (0)114 222 2262
E-mail: s.wharton@sheffield.ac.uk
Signature:
Date: 16/4/13



BNA2013:
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Speaker and Poster Abstracts

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Citations

The recommended citation for an abstract in this volume is as follows:

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Poster Ref: P1-B-066
Theme: Molecular, Cellular and Synaptic Mechanisms

Oxidative stress and DNA damage in white matter lesions of the human ageing brain

Sufana Al-Mashhadi[1], Julie Simpson[2], Paul Heath[2], Mark Dickman[2], Paul Ince[2], Stephen Wharton[2]
[1]*Sheffield Institute for Translational Neuroscience,* [2]*University of Sheffield*

Introduction: White matter lesions (WML), identified as hyperintensities on T_2-weighted magnetic resonance images (MRI) in the ageing brain, are linked to dementia and depression. Ischaemia, as well as other mechanisms, may contribute to their pathogenesis but the exact pathological role of these in WML remains poorly defined and the role of glial cell pathology remains unclear.

Aims: The current study investigates the hypothesis that oxidative DNA damage contributes to the pathogenesis of WML and the surrounding WM through altered glial cells functioning.

Materials and Methods: Expression of 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative stress, was investigated in WML and control WM, both from cases with WML (referred to as lesional controls) and without WML derived from the MRC-Cognitive Function and Ageing Study. Lesions were previously identified using post mortem MRI. Oxidative DNA damage was detected by immunohistochemisty and nuclear expression quantified as proportion of positive nuclei. Double staining was performed for GFAP, CD68 and oligodendrocyte specific protein to enable colocalisation of 8OHdG with markers of astrocytes, microglia and oligodendrocytes, respectively. Results: Extensive DNA oxidative damage was identified in all three groups of WM in multiple cell types. Both WML ($p=0.007$) and lesional control WM ($p=0.011$) showed significantly more 8-OHdG immunoreactive cells than control WM, whilst WML and lesional controls did not significantly differ ($p=0.526$). Other markers of DNA damage, including gamma histone H2AX (γ H2AX) and DNA dependant protein kinase (DNA-PK), showed a similar pattern of expression. Conclusion: Oxidised DNA is up regulated in ageing WM and may contribute to pathogenesis of WML. The similarity in the level of oxidative DNA damage in lesional control WM and WML suggests that oxidative damage is widespread and not confined to WML.

British Neuropathological Society meeting. London, March 2013

ing fibres is in keeping with the role of this molecule in muscle development.

Reference:

1. Morosetti *et al. Neurobiol Aging* 2010; **31**: 1205–14.

P17

Y.T. Asi[1,*], H. Ling[1,2,*], Z. Ahmed[1], A.J. Lees[1,2], T. Revesz[1], J.L. Holton[1]

[1]Queen Square Brain Bank, Department of Molecular Neuroscience, UCL Institute of Neurology, UK; [2]Reta Lila Weston Institute of Neurological Studies, UCL Institute of Neurology, London, UK; E-mail: yasmine.asi.09@ucl.ac.uk; *Shared first authorship

Cognitive impairment in multiple system atrophy: a clinico-pathological study

Introduction: Multiple system atrophy (MSA) is a progressive neurodegenerative disease characterized by parkinsonism, cerebellar ataxia and autonomic dysfunction. The pathological hallmark of MSA is glial cytoplasmic inclusions (GCI) found in oligodendrocytes with alpha-synuclein (αSyn) being the main constituent. Cognitive impairment has previously been regarded as an exclusion criterion in the diagnosis of MSA, but recent studies have shown that a proportion of patients with MSA do develop cognitive impairment.

Material and methods: Clinical data collected during life was retrospectively reviewed and 9 MSA cases (5 MSA-P and 4 MSA-C) with documented cognitive impairment (CI) and 9 matched MSA patients with normal cognition (7 MSA-P and 2 MSA-C) were selected from the archive of the Queen Square Brain Bank for Neurological Disorders (QSBB). αSyn, Ab, tau, GFAP, and TDP-43 immunohistochemistry and routine histological techniques were employed to determine neuronal and glial αSyn pathology, Ab deposition, tau pathology, gliosis, TDP-43 pathology and neuronal loss. Pathological changes were assessed using quantitative and semi-quantitative approaches.

Results: Neurons were well preserved in cortical and limbic regions of both the CI and non-CI groups. GCI burden was greater in cortical regions of the non-CI group, while it was greater in limbic regions of CI group, however, these findings did not reach statistical significance. Ab deposits were more frequent in the non-CI group, while Alzheimer-type tau pathology was no greater than Braak and Braak stage II in either group. Concomitant pathologies such as Lewy bodies, cerebral amyloid angiopathy, TDP-43 pathology and small vessel disease were uncommon in both groups.

Conclusions: Brain regions important for cognitive function did not show more severe neuronal loss or αSyn pathology in MSA patients with CI as compared with those with normal cognition. Alzheimer's disease and other secondary pathologies did not appear to have played a role in the cognitive decline in our MSA-CI group. Further explorations into synaptic pathology may explain the cognitive impairment observed in MSA.

Reference:

1. Gilman *et al. Neurology* 2008; **71(9)**: 670–6.

P18

S.A. Al-Mashhadi[1], J.E.Simpson[1], P.R. Heath[1], M.J. Dickman[2], P.G. Ince[1], S.B. Wharton[1]

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Oxidative stress and DNA damage in cerebral white matter lesions of the ageing human brain

Introduction: White matter lesions (WML), identified as hyperintensities on T2-weighted magnetic resonance images (MRI) in the ageing brain, are linked to dementia and depression. Ischaemia, as well as other mechanisms, may contribute to their pathogenesis but the exact pathological role of these in WML remains poorly defined and the role of glial cell pathology remains unclear.

Aims: The current study investigates the hypothesis that oxidative DNA damage contributes to the pathogenesis of WML and the surrounding WM through altered glial cells functioning.

Material and methods: Expression of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a marker of oxidative stress, was investigated in WML and control WM, both from cases with WML (referred to as lesional controls) and without WML derived from the MRC-Cognitive Function and Ageing Study. Lesions were previously identified using post mortem MRI. Oxidative DNA damage was detected by immunohistochemisty and nuclear

expression quantified as proportion of positive nuclei. Double staining was performed for GFAP, CD68 and oligodendrocyte specific protein to enable colocalisation of 8OHdG with markers of astrocytes, microglia and oligodendrocytes, respectively. Expression of Malonaldehyde (MDA) was also quantified as a marker of lipid peroxidation using Western Blotting technique on the frozen cohort.

Results: Extensive DNA oxidative damage was identified in all three groups of WM in multiple cell types. Both WML ($P = 0.007$) and lesional control WM ($P = 0.011$) showed significantly more 8-OHdG immunoreactive cells than control WM, whilst WML and lesional controls did not significantly differ ($P = 0.526$). Other markers of DNA damage, including gamma histone H2AX (H2AX) and DNA dependant protein kinase (DNA-PK), showed a similar pattern of expression. MDA quantification did not significantly differ between the three groups of WM. However, similar to 8-OHdG's statistical analysis, lesional Control group showed the highest and widest spread of lipid peroxidation.

Conclusions: Oxidised DNA is up regulated in ageing WM and may contribute to pathogenesis of WML. The similarity in the level of oxidative DNA damage in lesional control WM and WML suggests that oxidative damage is widespread and not confined to WML.

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L. Parkkinen, C. Joachim, M.M. Esiri, O. Ansorge
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Relationship of Apolipoprotein E to Parkinson's disease-related alpha-synuclein pathology

Introduction: In addition to widely recognised association between apolipoprotein (ApoE) and Alzheimer's disease (AD), this gene has also been suggested to be a risk factor for Parkinson's disease (PD), and especially influence the dementia in PD. A massive increase of ApoE levels is also seen in transgenic mice with α-synuclein-induced neurodegeneration.

Material and methods: We aimed to examine whether ApoE possible determinant of PD-related alpha-synuclein pathology independent of frequent concomitant AD pathology in large prospective aging study Oxford Project to Investigate Memory and Aging (OPTIMA).

Results: Frequency of ApoE polymorphisms was significantly different (Chi-square, $P = 0.016$, df=4) between 125 OPTIMA cases with alpha-synuclein pathology (ε2/ε3 8%, ε2/ε4 5.6%, ε3/ε3 34.4%, ε3/ε4 37.6%, ε4/ε4 14.4%) and 293 cases without (ε2/ε3 9.9%, ε2/ε4 2.4%, ε3/ε3 47.8%, ε3/ε4 32.8%, ε4/ε4 7.1%). The allelic frequency of ε4 showed a significant increase with progressive PD stages but this disappeared when adjusted to AD-related pathology.

Conclusions: Our results do not support the independent determinant role of ApoE in the progression of PD pathology but we need to examine the association to cortical Lewy body load in more detail.

P20

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A previously unrecognised fatal bovine tauopathy is present in aged cattle throughout the UK

Introduction: A number of tauopathies are recognised in man but only thread-like tau accumulations of uncertain clinical significance have been reported in senescent animals and experimental animal disease. Since 1986, an idiopathic neurological condition of adult cattle has been recognised in the UK as a sub-set of cattle slaughtered as suspect BSE cases. This disorder is characterised by brainstem neuronal chromatolysis and degeneration with variable hippocampal sclerosis and spongiform change.

Material and methods: Selected cases of idiopathic brainstem neuronal chromatolysis (IBNC) were identified from archive material and characterised neuropathologically. These were labelled for tau using antibodies AT8, and tau antibodies specific to threonine (T) T205, T212, T231, and serine (S) S214, S396 S404 and RD3 and RD4 which recognises a microtubule binding region. Labelling was also carried out for synuclein, TDP43, Aβ1-42, Aβ1-40.