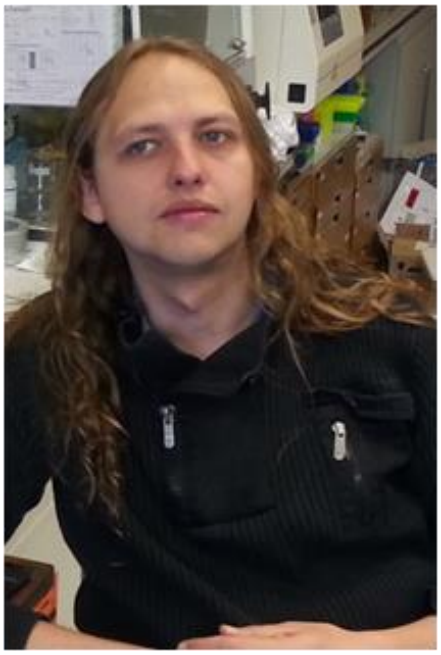

Name and job description

Dr David Koss, Postdoctoral Research Fellow, working in the lab of Professor Bettina Platt.

What disease area do you specialise in?

My main research interest is Alzheimer's disease, but my focus on tau pathology means I have also investigated some issues relevant to related tauopathies.

What is your project about?

The project, led by myself and Professor Platt, aims to assess the correlation of traditional Alzheimer's pathology (amyloid and tau), with the occurrence of an endoplasmic reticulum stress response – known as the unfolded protein response. To do this I've used human brain tissue, comparing pathologically confirmed Alzheimer's cases with healthy age matched control samples. To date we have evaluated existing protocols and developed new tools for the quantification of amyloid and tau pathology. Through a collaboration with Dr Mirela Delibegovic, we are also developing markers for the unfolded protein response.

Building upon our established data set (at present, comprising of 27 markers) we have now been able to correlate our experimental quantifications of amyloid, tau and the unfolded protein response with a range of cognitive scores, further pinpointing particular markers of interest from their correlation with cognitive deficits.

We are currently finalising a few data sets before publishing the first findings of our work. Now we aim to look downstream of the unfolded protein response in these well characterised brain samples, specifically focusing on autophagy and apoptosis. In addition we hope that this project will attract funding for a new PhD project to be supervised by Professor Platt and myself.

What brain regions did you request?

We received samples from 51 cases in total – both Alzheimer's and healthy age-matched controls. With advice from BDR, we requested temporal cortex, more specifically Brodmann's area 21. The region becomes affected with tau pathology in Braak stage 3. The mid stage involvement of this region means that samples from individuals below this pathological score act as a good contrast to those with mid or late stage pathology. This is quite important as it is likely that some of our "non-AD" cases, are indeed prodromal for the disease. Accordingly, however, the detection of novel markers prior to the onset stage (Braak3) may indeed indicate their early occurrence in the disease progress and thus may suggest a causative role for such marker.

How has BDR tissue contributed to your work?

BDR tissue has undoubtedly been critical to allow us to conduct this project. The use of human disease samples is essential when validating novel molecular pathways potentially involved in Alzheimer's disease pathology and cannot be replaced by the use of any experimental model. We have found BDR incredibly helpful in advising us, in terms of sample preparation, realistic expectations as regards the ability to detect signals in post-mortem samples and in attempting to meet our requests for tissue whenever possible.

How easy was it to get tissue from BDR?

During the preparation of our project grant, we wrote an email outlining our requirements of frozen and fixed tissue, together will some enquires regarding the availability of cognitive and biographical information. From this initial contact, we were sent a form for an official request requiring some additional project details. Once our project was successfully funded, we were pleased to discover that upon approval from the BDR, no additional ethics approval was needed as the work was covered by BDR's ethical remit. Furthermore, in conjunction with our own in-house health and safety committees, the brain bank advised us on safety procedures and best practice when handling this tissue as well as safe sample storage.

Receipt of the samples did require some organisation. As we received tissue from the Oxford Brain Bank, The MRC London Neurodegenerative Diseases Brain Bank, the South West Dementia Brain Bank, Manchester Brain Bank and the Newcastle Brain Tissue resource, individual material transfer agreements were required. However given the scope of our request we appreciate that this was necessary.

What were the benefits of using BDR tissue?

The benefits of being fortunate enough to use this resource have been vast. Personally as an Alzheimer's researcher for nearly ten years, working with human tissue has prompted a rethink on my understanding of the disease. At a time where most labs rely on well-defined and controlled disease models, I think it's important to be reminded that these are indeed just models and do little in way of recapitulating the diversity and complexity found in human lives which may indeed contribute to the disease. I believe it is essential that many more research groups consider complementing their work with resources from BDR. For our work, detecting and validating molecular findings determined in our experimental models within these samples has enabled us to focus on truly translational research. Likewise the detection of novel markers in human samples has allow us to back translate these finding into our experimental models, where further investigation can be conducted in a more controlled situation.

We are extremely grateful to those individual and their families who realise the importance of being able to provide such invaluable resources, from which treatment of this disease can be greatly improved.