



The PSP Association's International Medical Workshop 7th July 2009

ABSTRACT

Title of Talk: LITHIUM AND GSK INHIBITION: DISEASE MODIFICATION FOR PSP?

Part 1: Speaker(s) details	
Title	Professor
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Part 2: Abstract (Maximum 400 words) Please make your abstract easy to understand as it will appear on our website and will be read by people with PSP and their carers who are not scientists but who will want to understand your work and what it means for them.

Hyperphosphorylation of a structural protein called tau is believed to be key in the sequence of events leading to cell death in PSP, as well as a number of other neurodegenerative diseases. Tau is a microtubule associated protein that helps to scaffold the cell's internal structure.

Glycogen synthase kinase 3 β (GSK-3) is an enzyme associated with hyperphosphorylation of tau. Over-expression of this enzyme in animal models leads to behavioural impairments and neurodegeneration. Inhibition of this enzyme is therefore a logical approach to prevent disease progression in a range of "tauopathies", including PSP.

Lithium is a soft, silvery, reactive metallic element found naturally as lithium carbonate. Lithium was approved by the FDA in early 1970s for treatment of bipolar mood disorder. More recently interest has turned to the GSK-3 inhibiting properties of this agent, and its possible ability to benefit Alzheimer's disease, PSP and related disorders. Lithium is not an easy drug to use, by virtue of its toxic effects at high plasma levels.

The PSP (Europe) Association recently, in conjunction with the National Institute for Health (US), funded a trial to investigate whether people with either PSP or the closely related condition, corticobasal degeneration, could take lithium safely, and tolerate any potential side effects. The trial only needs to recruit 45 subjects to achieve this aim. It will also provide preliminary data regarding the effect that lithium might have on blood and CSF markers, as well as clinical features. The trial is currently ongoing, and will inform whether future larger studies based on clinical effectiveness as an outcome measure, should be performed.

Another GSK-3 inhibitor, NP060103, derived from a screening programme of marine extracts, is also about to enter clinical trial in Europe, led by Noscira, a Spanish-based Research and Development Company.

From the bleak horizon of a few years ago, these are exciting times for PSP therapeutic research, so often overlooked previously by "big Pharma". The research infrastructure that will be generated in the course of the GSK-3 inhibitor trials will also provide longer term benefits for PSP trial work in general.