In a study by Karlamangla and colleagues, researchers measured the resting overnight urinary cortisol levels of 538 individuals (55% female, 45% male) aged 70–79 years with high cognitive function. Neuropsychological testing was used to assess their baseline cognitive function, and follow-up testing was carried out 3 and 7 years later to assess any changes. Cortisol measurements for participants were divided into quartiles for analysis.

Those in the upper three quartiles were found to be at higher risk of incident cognitive impairment than those in the lowest quartile (16% vs 9%), with similar risks for men and women. Adjustment for potential confounders, such as age at baseline, did not greatly affect the association.

In a separate study, Li *et al.* collected salivary cortisol samples from 79 cognitively intact participants aged 63 years or over. Samples were taken at 08:00 h, 15:00 h and 23:00 h, and the procedure was repeated annually for 3 years. Neuropsychological tests were carried out 2–3 days after collection of samples. For the 46 participants (52% female, 48% male) who completed the study, a higher baseline cortisol concentration at 23:00 h predicted a decline in memory as measured by delayed paragraph recall performance.

In the effort to develop strategies for halting cognitive decline in older adults, it is suggested that further research should be undertaken to develop methods of attenuating the detrimental effects of higher cortisol levels in this population.

Christine Kyme

Original articles Karlamangla AS *et al.* (2005) Urinary cortisol excretion as a predictor of incident cognitive impairment. *Neurobiol Aging* 26 (Suppl): S80–S84
Li G *et al.* (2005) Salivary cortisol and memory function in human aging. *Neurobiol Aging* [doi: 10.1016/j.neurobiolaging.2005.09.031]

The genetic and clinical phenotype of *LRRK2*-associated familial PD

Disease-causing mutations in *LRRK2*, a novel gene that encodes the protein dardarin, have been reported in large kindreds with autosomal dominant Parkinson's disease (PD). Khan and colleagues performed a detailed study of the *LRRK2* phenotype, neuropathological data, functional imaging and olfactory testing on the largest British kindred (the Lincolnshire kindred) known to have late-onset, familial PD associated with such a mutation. They also screened a further 117 unrelated patients with familial PD to identify common and novel mutations.

Kindred patients shared the Y1699C mutation in *LRRK2* and showed asymmetrical, levodopa-responsive parkinsonism with unilateral leg tremor at onset and foot dystonia. Cognition was generally unaffected despite lengthy disease duration, although there was a prominent behavioral disorder in seven patients in the kindred. Mean age of onset was 58.8 years (range 40–75 years) and successive generations showed a lower age of onset.

A mutation screen of all 51 exons of *LRRK2* in 117 subjects from other smaller British kindreds with familial PD identified G2019S as the most common mutation (overall frequency 2.5%). Two novel mutations, R1941H and T2356I, were also identified.

The authors conclude that *LRRK2* probably represents the most common locus for mutations in patients with autosomal dominant PD. The clinical phenotype of *LRRK2*-associated PD is similar to that of idiopathic, late-onset PD. Further studies into the role of dardarin in PD are required.

Carol Lovegrove

Original article Khan NL *et al.* (2005) Mutations in the gene *LRRK2* encoding dardarin (PARK8) cause familial Parkinson's disease: clinical, pathological, olfactory and functional imaging and genetic data. *Brain* 128: 2786–2796