Impaired sense of smell may be early indicator of Parkinson's disease

March 20 2008

Impaired sense of smell occurs in the earliest stages of Parkinson's disease (PD) and there is mounting evidence that it may precede motor symptoms by several years, although no large-scale studies had confirmed this. In the first study involving the general population, researchers found that smell impairment can precede the development of PD in men by at least four years. The study is published in the *Annals of Neurology*.

Led by G. Webster Ross of the VA Pacific Islands Health Care System and the Pacific Health Research Institute in Honolulu, Hawaii, the study included 2,267 men from the Honolulu-Asia Aging Study who received olfactory testing at least once, either between 1991 and 1993 or between 1994 and 1996, and were followed for up to eight years to find out if they developed PD. During the course of follow-up, 35 men developed the disease.

The results showed that an odor identification deficit can predate the development of PD by at least four years, although it was not a strong predictor beyond this time period. Decreased odor identification was associated with older age, smoking, more coffee consumption, less frequent bowel movements, lower cognitive function and excessive daytime sleepiness, but even after adjusting for these factors, those with the lowest olfactory scores, meaning they had the poorest odor identification, had a five times greater risk of developing PD than those with the highest scores.

“One interpretation of this finding is that the relationship of olfactory deficits to higher risk of future PD begins to weaken beyond a threshold of approximately four years between testing and diagnosis,” the authors state. The fact that the time from olfactory testing to diagnosis was shortest among those with the lowest olfactory scores supports this. In addition, findings from earlier studies suggest that olfactory impairment begins between two and seven years prior to diagnosis, and estimates from neuroimaging and pathological studies suggest that there is a period of about five to seven years between the onset of nerve loss in an area of the brain affected by PD and diagnosis of the disease.

The pathology of smell impairment in PD is not completely understood, but nerve loss and the formation of Lewy bodies, abnormal clumps of proteins inside nerves cells that are thought to be a marker of PD, are known to take place in the olfactory structures of patients with the disease. The authors note that one study involving brain dissection of deceased patients with neurological disease found that olfactory structures are the earliest brain regions affected by Lewy degeneration, which supports the idea that an impaired sense of smell could be one of the earliest signs of the disease. Olfactory deficits in PD may be caused by impaired nerve cell formation.The olfactory bulb is one of two regions in the brain that receives new neurons throughout life, and dopamine depletion, which occurs in PD, has been shown to impair nerve cell growth in this structure in rodents. It may also be that olfactory deficits are not directly related to the structures themselves, but originate in the amygdala, an area of the brain affected by PD that is known to be involved in smell function. An impaired sense of smell could also be caused by impaired sniffing, which may be another motor symptom of PD.

The authors conclude, “Olfactory testing along with screening for other potential early indicators of PD such as constipation or sleep disturbances could provide a simple and relatively economic means of

identifying individuals at high risk for developing PD who could participate in trials of medications designed to prevent or slow disease progression." The study is located at Kuakini Medical Center in Honolulu.

Source: Wiley