SUMMARY

Background

The mainstay of the pharmacological treatment of Parkinson's disease (PD) is levodopa therapy, although the associated long term side effects of motor fluctuations and dyskinesias are well recognized. In recent times, hyperhomocysteinemia (HHcy) has emerged as a long term complication of levodopa therapy in the treatment of PD. HHcy is associated with increased cardiovascular risk and has been identified as a risk factor for cerebrovascular disease, dementia, and depression. Evidence from some recent studies has established a relationship between hyperhomocysteinemia, cognitive impairment and disease severity in PD. There is sparse information on the frequency of HHcy in Africans with PD, and the effect of HHcy on disease outcome.

Objective

The study hypothesis was that hyperhomocysteinemia is frequent in African patients with PD, and contributed to worsened disease severity, disability, cognitive function and depression. The aims of the study were thus as follows: (a) determine the frequency of HHcy in Nigerian PD patients attending the Lagos University Teaching Hospital; (b) determine the relationship between HHcy and disease severity and disability using the Hoehn and Yahr staging, and the Unified Parkinson’s Disease Rating Scales Motor Scores and Activities of Daily Living Scores; (c) determine the relationship between HHcy and cognitive function using the MMSE and Category Fluency Test Scores; and (d)
determine the relationship between HHcy and depression using the Zung Self-rating depression scale (ZSDS).

**Methodology**

A total of 40 patients with Parkinson’s disease attending the Lagos University Teaching Hospital, Idi- Araba Lagos, and 40 apparently healthy, age-, sex- and educationally-matched controls, were studied. The disease characteristics (age at onset, age at diagnosis, age at time of study, disease duration) and treatment characteristics (treatment category, levodopa dose in 24hours, duration of levodopa therapy) were obtained by direct questioning and review of case records. Quantitative rating of disease severity [using the Unified Parkinson Disease Rating Scale (UPDRS) motor score and the Hoehn and Yahr stage] and disability [using the UPDRS activities of daily living (ADL) score] was conducted. Cognitive function was assessed using the minimental state examination (MMSE) and category fluency test. Depressive symptomatology was assessed using the Zung Self-depression Rating Scale (ZDRS). Venous blood samples for homocysteine (Hcy) estimation were taken in the fasting state from all the study subjects.

The frequency of HHcy was compared between the PD cases and healthy controls and between the PD cases on levodopa therapy and PD cases that were levodopa naïve. Cognitive performance, presence of depressive symptomatology, disease severity and disability were also compared between the PD cases with HHcy and those with normal Hcy levels.
**Results**

The mean age of the PD cases was 65.8 ± 9.8 years and this was not significantly different from the mean age of the controls which was 63.3 ± 10.8 years (p = 0.27). Both the PD cases and the control group were made up of 32 males and 8 females giving a male to female ratio of 4:1 for both cases and controls.

The mean Hcy levels were similar in the PD cases (13.8 ± 5.4) and controls (12.4 ± 3; p>0.05). In all, 14 (35%) of the PD cases and 11 (27.5%) of the controls had HHcy. Among the PD cases, 14/35 (40%) of those on levodopa (LD) treatment had HHcy compared with none 0/5 (0%) of the levodopa naïve PD cases (P>0.05). Mean Hcy levels for the subgroup of PD cases on levodopa (LD) for long duration (> 24 months) (15.6 ± 6.5) was however significantly higher than the mean Hcy level of the control population (12.4 ± 2.3) (p = 0.02). The PD cases with HHcy tended to be on LD treatment for a longer duration than the cases with normal Hcy levels (72.9 ± 88.2 months versus 32.9 ± 34.7 months; p = 0.06).

There was no significant difference in measures of disease severity and disability between the PD cases with and without HHcy (p>0.05 in all instances). However, the trend was that of poorer scores in the PD cases with HHcy. Median Hoehn and Yahr score in the cases with HHcy was 2.5 compared with 2.0 in the cases without HHcy. Mean UPDRS motor score was 43.9 ± 16.2 in the cases with HHcy compared with 39.7
± 18.4 in the cases without HHcy (p = 0.3). Mean UPDRS ADL score in the PD cases with HHcy was 15.1 ± 8.0 compared with 12.7 ± 6.7 in those without HHcy (p = 0.4).

Cognitive profile using the modified minimental examination (MMSE) scores was similar between the PD cases with HHcy and those with normal Hcy levels- 26.2 ± 1.6 versus 26.0 ± 3.3 (p = 0.6). However PD cases with HHcy performed significantly worse using the category fluency test compared with controls – 8.0 ± 2.2 compared with 10.8 ± 3.5 (p = 0.009). There was no significant difference in depressive symptomatology using the ZDRS score between PD cases with HHcy (41.5 ± 7.0) and those with normal Hcy levels (40.0 ± 11.4) (p = 0.7).

**Conclusion**

Hyperhomocysteinemia occurs more frequently in Nigerian patients with Parkinson’s disease who are on levodopa treatment compared with age, sex and educationally matched controls. HHcy is more likely to occur in PD cases on levodopa following long duration of therapy (>24 months). Cognitive impairment may be worse in PD cases with HHcy as demonstrated using the Category Fluency test.