Measurement of caudate nucleus area –
A more accurate measurement for Huntington’s disease?

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Summary. Caudate nucleus atrophy occurs in Huntington’s disease and methods of measuring this have been described using axial CT, but these are indirect and lack sensitivity. We measured caudate nucleus area (blind to the subjects’ clinical state) in 30 subjects with or at risk of Huntington’s disease, and in 100 normal age matched controls. Fifteen subjects with established symptomatic Huntington’s disease, 3 with early symptoms, and 3 presymptomatic subjects (2 showing a high probability for the Huntington’s disease gene on genetic testing, and one who has since developed symptoms) were correctly identified. Three normal (gene negative) family members were also correctly identified. Outcome is awaited in 6. CT caudate area measurement is simple and reproducible and we have found it to be a useful confirmatory test for Huntington’s disease.

Key words: Huntington’s disease – Caudate nucleus – Chorea

Huntington’s disease (HD), with autosomal dominant inheritance, is characterised by insidious onset in adult life of severe progressive cognitive impairment, choreiform movement disorder, and psychiatric disturbance [1]. The pathological changes are global cerebral atrophy due to neuronal loss, predominantly affecting the caudate nucleus (CN) and putamen [2]. The cause of this is unknown. The severity of neuronal loss [3], the type and rate of progression of symptoms, and age of onset all vary [4]. In a subject showing the classical features of HD, the diagnosis is usually clearcut, but presentation in childhood or old age, with an unusual pattern of symptoms, or without any family history, can make the diagnosis more difficult. Most subjects coming from affected families are acquainted with its devastating effects, and would like to know their HD status before starting a family [5]. There is no positive diagnostic test yet for HD, as the HD gene itself has not yet been identified [6]. Thus the results of genetic testing can only be expressed as a probability of having (or not having) the HD gene, and appropriate family members must also be available for study.

CT brain scanning has been found useful to exclude other causes of symptoms similar to HD. Cerebral atrophy with disproportionately small caudate nuclei may be visible, or the brain may appear normal. Methods of quantifying the caudate atrophy have been described, notably the bicaudate ratio [7-9] and the ratio of the distance between the tips of the frontal horns of the lateral ventricles (FH) to the distance between the caudate nuclei (CC) at the foramen of Munro [10-13]. These are linear measurements of volume loss (Fig. 1), are indirect, and relatively nonspecific. They have not been shown to be of value in presymptomatic detection of affected individuals [12, 13]. PET [14, 15], SPECT [17] and MRI [16] are also capable of detecting caudate abnormalities but are not widely available.

On axial CT, measurement of caudate area would seem to be a more direct measure of caudate atrophy, and we therefore undertook this study of a mixed group of patients referred from the HD clinic. Normal range of cau-
Fig. 2. CT scan of drawing around caudate - asymptomatic DNA positive subject with small caudate area

Fig. 3. CT scan of definite abnormal caudate area in symptomatic subject

Fig. 4. CT scan of definite normal caudate area in DNA negative subject

date size was established by measurements taken from 100 normal CT brain scans.

Method

Subjects either had symptoms of HD (early or established) or were asymptomatic but with a positive family history. All were assessed by an experienced clinical geneticist. Where possible genetic testing was performed. Many patients, usually those with early symptoms or in whom there was some doubt about the diagnosis of HD, were assessed by a clinical neuropsychologist, and had detailed neurological and psychological testing according to the Baltimore Huntington's disease protocol [18]. This enables the patient's clinical features to be 'scored' and helps discriminate HD from other dementias with movement abnormalities.

All subjects had an axial CT brain scan (GEC 8800) without contrast, in 10 mm intervals from base of skull to vertex, with additional images at 3 mm intervals through the caudate nuclei. The CT scans were analysed at standard settings by the authors without knowledge of the subjects' clinical details (window width 80, level 40 HU). The areas of the right and left heads of the caudate nuclei were traced, (using the cursor and 'area of interest' function available on the CT consul) by drawing on the point of maximum contrast change between the caudate and adjacent brain or CSF (Fig. 2). In practice, this edge was easily identified without image edge enhancement [19]. The caudate areas were measured on all slices on which they were visible, and the largest measurement for each nucleus was used for analysis.

The FH and CC distances were measured on all slices using the CT consul functions, noting which was at the level of the foramen of Munro. Each measurement was performed 3 times. For the control group, caudate area, FH and CC distances were measured on 100 CT brain scans of patients aged 10 to 70 years, performed for the investigation of migraine, TIA's or other benign neurological conditions and judged normal by one of two neuroradiologists.

Intraobserver error was calculated from repetitive area and distance measurements, and interobserver error for the authors was calculated by comparing their measurements in a subgroup of patients. We found 10% variation in area and distance measurements both within and between authors, and felt that this was acceptable.

Results

Normal caudate area decreases with age (Table 1) as one might expect, from age-related changes, and similarly the FH:CC ratio also decreases. The limits of normality were defined as the mean ±2 standard deviations, and therefore caudate area of less than 1 cm² was considered abnormal. Our normal values for FH:CC ratio agreed closely with previous studies [10–13], a value of less than 2.0 being considered abnormal. Thirty subjects with or at risk of HD had a CT brain scan. At the time of CT, 15 had definite established HD, 10 were asymptomatic and 5 had possible early symptoms of HD. There were 18 males and 12 females. Ages ranged from 22 to 67 years, and duration of symptoms from 0 to 16 years (mean of those with established symptoms was 3.5 years).

| Table 1. Normal caudate area measurements and FH:CC ratios by decade |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age (yrs) | No. in group | Right caudate area cm² (mean ± 1 SD) | Lower limit of normal | Left caudate area cm² (mean ± 1 SD) | Lower limit of normal | FH:CC (mean ± 2 SD) |
| 10–29 | 21 | 1.39 ± 0.18 | 1.03 | 1.33 ± 0.16 | 1.01 | 3.62 ± 0.82 |
| 30–39 | 26 | 1.27 ± 0.12 | 1.03 | 1.23 ± 0.14 | 0.99 | 3.35 ± 0.70 |
| 40–49 | 30 | 1.27 ± 0.16 | 0.95 | 1.23 ± 0.14 | 0.95 | 3.15 ± 0.50 |
| 50–59 | 23 | 1.24 ± 0.20 | – | 1.25 ± 0.19 | – | 3.16 ± 0.56 |