Pneumoencephalographic planimetry in neurological disease

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The outline of the ventricular system on the pneumoencephalogram (PEG) can be easily measured and lends itself to quantification. Several methods have been developed which utilize linear measures of the ventricles, or ratios of ventricle to skull size. Planographic measurements of the area of the ventricles have been employed in a few studies, but have generally been dismissed as too cumbersome for use (Bruij, 1959).

While a number of previous investigators have related quantitative PEG findings to clinical neurological and psychometric data, most studies have suffered from one or more limitations. Studies reporting measurements on a large number of PEGs have usually been limited in amount and specificity of clinical information, often to such general statements as to the presence or absence of 'dementia'. For instance, Lönnnum (1966) carefully measured PEG films, but was able to correlate such data only with 'the degree of impairment at work and in social life'. On the other hand, studies reporting detailed behavioural observations typically have employed relatively small experimental groups (Kiev, Chapman, Guthrie, and Wolff, 1962). Within these extremes, considerable variation in results is reported. Burhenne and Davies (1963) found a good correlation between ventricular size and 'dementia', while Larsby and Lindgren (1940) found no correlation between mental changes and the PEG. Studies relating ventricular size to findings on clinical neurological examination other than 'dementia' typically have been limited to a single aetiological or diagnostic classification (Larsby and Lindgren, 1940; Davies and Falconer, 1943; Gath and Vinje, 1968; Selby, 1968) or have preselected patients on the basis of highly deviant findings (Hunter, Hurwitz, Fullerton, Nieman, and Davies, 1962). In addition, the absence of adequate PEG data on a control population has been a limiting factor.

In the present investigation planographic rather than linear measures of ventricular size were used. The subjects were not selected on the basis of a particular aetiology nor on the basis of presence or absence of asymmetry of the lateral ventricles. Detailed clinical and electroencephalographic data were available on all subjects for purposes of diagnostic classification, and, in addition, a standardized battery of neuropsychological tests providing quantitative measurement of intellectual and motor-sensory status was administered to the majority of the subjects. PEG data on a group of subjects without clinical, neurological, or electroencephalographic evidence of neurological disease were also included for comparison purposes. The present report describes the ventricular measurements in relation to clinical classification and neurological examination findings. The results of the analysis of the neuropsychological test data will be reported in a subsequent paper.

METHODS

CLINICAL All PEGs performed by the Department of Neurology, University of Wisconsin from 1963-67 were reviewed. Those subjects who showed no evidence on the PEG of an intracranial tumour or other lesion which distorted the ventricular topography were selected for further review. Only those subjects who had no clinical evidence after review of their medical records of increased intracranial pressure were included in the final study. The 86 subjects who were identified by these criteria in whom PEG films were of sufficient quality to permit accurate measurement, and in whom adequate clinical data were available, thus represent examples of non-surgical neurological disease.

Thirty-six of these subjects suffered from chronic recurring epileptic seizures of unknown cause. Fifteen of these had generalized major or minor seizures, while 21 had focal cortical seizures of which 16 were psychomotor in type. This group will be referred to as the 'epilepsy group'. In another 36 subjects a more specific or primary neurological diagnosis could be established, even though several members of this group had seizures as a complication of their primary disease. This group will be

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referred to as the 'neurological' group. Eight subjects in this group suffered from heredo-degenerative disease syndromes (spinal cerebellar degenerations, Wilson's disease, Parkinsonism, etc.). An additional seven subjects represented cases of post-traumatic encephalopathy. Definite or probable multiple sclerosis was diagnosed in six members of this group, while five subjects suffered from either completed infarction or transient reversible ischaemic attacks. Chronic encephalopathy secondary to viral encephalitis or bacterial meningitis was present in three subjects, and one subject was luetic. A chronic brain syndrome of unknown cause was present in three, while alcoholism associated with a chronic brain syndrome was present in two subjects. One subject had suffered a prolonged period of cerebral anoxia. Seven subjects from the University of Wisconsin sample could not be reliably assigned to any of the diagnostic groups including the non-neurological group to be discussed below. The PEG measurements from these seven subjects were included in the determination of the overall ventricular size and symmetry data, but these subjects were excluded from all analysis relating PEG measurements to various clinical and case history findings.

Review of the medical records, neuropsychological test results, and electroencephalograms of seven additional subjects from the University of Wisconsin revealed no evidence of neurological disease. These subjects were assigned to the 'non-neurological' group. In order to increase the size of the non-neurological group, all PEGs on file in the radiology department of a large penal institution were reviewed. Initial selection from the prisoner sample was based upon the radiological criteria of absence of evidence of a mass lesion, regardless of other size or symmetry characteristics of the lateral ventricles. Of the individuals so identified only subjects with a current medical history, neurological examination, and EEG performed by the authors were included in the final study. In both the prison sample and the patients from the University of Wisconsin, a history of major or recurrent head injury, prolonged or excessive use of alcohol, or unexplained loss of consciousness was sufficient for exclusion from the non-neurological group, as was any abnormality on the EEG or clinical examination. Eighteen subjects from the penal institution were found who met these clinical criteria. The majority of these subjects were studied originally because of a complaint of headaches. Several carried primary psychiatric diagnoses, but none had features of an organic brain syndrome. Obviously the subjects from the penal institution had been convicted of some breach of the legal code, and no claim is made that these 25 subjects represent a normal population. Instead we have chosen to designate them as a non-neurological group in contrast with the 72 subjects in whom definite neurological abnormality was present, including epilepsy of unknown cause.

The results of the neurological examination were recorded for each subject. Subjective complaints were not assessed as positive unless they were accompanied by objective findings. Isolated abnormalities such as increase in muscle stretch reflexes in one body member were not scored as positive unless they were accompanied by loss of function, weakness, pathological reflexes, or sensory changes. Subjects with a diagnosis of chronic brain syndrome were assigned to the primary neurological group but were scored as having a normal neurological examination unless lateralizing motor or sensory findings were present. Thus the examination abnormalities recorded are those revealed by the motor and sensory assessment techniques of the conventional neurological examination. For each subject, the results of the examination were summarized as within normal limits, or as showing predominantly unilateral or bilateral abnormality. Intellectual functioning, including psychometric intelligence levels and abstraction-concept formation ability was assessed by a standardized battery of neuropsychological tests administered to all subjects from the University of Wisconsin sample.

**Radiological methods** All PEGs had been performed by the partial exchange technique in which 25 to 80 ml of air was exchanged for varying amounts of spinal fluid. The brow-up anterior-posterior projection was used. Target to film distance was 36 in. for all films. The area chosen for measurement was the cella media. Tracings were made on paper, and the planographic and linear measurements were made from the tracings. Examples of the tracings of the cella media are shown in Figure 1.

All measurements were made by the same individual. Each ventricle was measured at least three times and the average of the several readings was taken as the score for that ventricle. Linear measures used were the septal-caudate line (36 subjects), the ventricular span (50 subjects), and the greatest transverse diameter of the cella media measured parallel to the roof (50 subjects). The measurements used are illustrated in Figure 2.

The area of the cella media was measured by the use of a planimeter, a simple instrument that mechanically integrates a trace of the perimeter of an object into the area of the object. The instrument used reads the area...
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directly in square inches to two decimal places. The readings were converted to square centimetres and rounded to the nearest 0.1 cm². The reliability of the planographic measurement was evaluated by repeating the measure in 27 subjects, chosen randomly and without knowledge of the original measurement. The first and repeat measurements were compared. The average error of the linear measures on repeat determination was less than 3%.

The effect of rotation in the lateral plane upon the planographic measurement was assessed by comparing the measurements from a relatively true AP projection in 19 subjects with similar measurements from a film deviated approximately six degrees to the right or left of the midline for the same subject. These films had been originally taken for stereo viewing. The average difference of measurement was 4.3%.

In the 'normal' projection for our laboratory, the petrous ridge is seen near or slightly below the centre of the orbit, and variation of the horizontal axis can be detected by changes in this relationship. Measurements were compared in 15 subjects, not included in the final study, in whom two films were available but with markedly different horizontal axis. An average difference of 8.5% was obtained. All measurements included in the final study were taken from films which by inspection were well within the limits of horizontal and lateral deviation employed in these control determinations.

As an additional test of the reliability of the planographic measures, the following study was carried out. Twelve patients without clinical or radiological evidence of a mass lesion, not included in the final study, and in whom more than one PEG had been performed, were identified. Most of these subjects had undiagnosed disease of the central nervous system with slow but definite progression of their condition. The repeat PEG had been performed to help establish a more definitive diagnosis. The interval between procedures ranged from two weeks to 12 years, with an average of 3.5 years. Five of the 12 comparisons were based on PEGs which were separated by intervals of five or more years. An average increase in size of the lateral ventricles of 8.8% was found. The error of measurement and the effect of rotation undoubtedly contributed to some of this variance, since it was difficult to find films of exactly the same projection from both procedures in all subjects.

For both the planographic and linear measures, asymmetry of the lateral ventricles was expressed as a ratio obtained by dividing the score for the smaller by the larger ventricle for each subject and multiplying by 100. The resultant figure can be considered a percent of symmetry, with the smaller percentages representing the greatest asymmetries, and with 100% representing perfect symmetry.

RESULTS

Planographic measurements of the cella media of individual ventricles ranged from 1.2 to 10.7 cm³, with a mean of 3.3 cm³ for the total sample of 208 ventricles. The score obtained by summing the right and left ventricle measurement for each subject ranged from 2.4 to 17.7, with a mean of 6.6 cm³. Symmetry ratios ranged from 30 to 100% with a mean of 85%.

Table I shows the means and ranges of ventricular size and symmetry as a function of age. A consistent increase in size of the ventricles with age was noted, with this change most marked in the older groups. While the overall inter-group difference in mean ventricular size for the five age classifications was significant at the 0.01 level of confidence, inspection of the ranges given in Table I shows that considerable variation was present within all age groups. In contrast with the significant F ratio found on total ventricular size, no significant differences in symmetry ratios by age were found in these same groups. No difference in mean ventricular size or symmetry was present between males and females.

Table II summarizes the ventricular measurements of the separate clinical groups. The score obtained by summing the planographic measurement of left and right ventricles in each subject was used for the analysis of ventricular size and clinical results.

<p>| TABLE I |</p>
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<th>VENTRICLE MEASUREMENTS AND AGE</th>
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<tr>
<td><strong>Age (yr)</strong></td>
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<td><strong>mean (sq. cm) range</strong></td>
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<td>15-20</td>
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| F = 4.43 | F = 0.1 |
| P < 0.01 | NS |
The overall difference in mean combined ventricular size for the three groups was significant beyond the 0.001 level. Individual t tests revealed that the significant variance was contributed by the neurological group, which differed from both the epilepsy and non-neurological groups beyond the 0.001 level. No difference was found between the non-neurological and epilepsy groups. The mean symmetry differences among the three clinical groups were less marked, but the associated F ratio was nevertheless significant at \( P < 0.01 \). The only significant intergroup difference was between the neurological and non-neurological group \( (P < 0.01) \) with the epilepsy group showing symmetry ratios intermediate between the other two.

Table III presents mean combined ventricular measurements as a function of duration of illness for subjects from the epilepsy and neurological groups. The classification used, while arbitrary, represents subjects with short (two years or less), intermediate (three to 10 years), and long-term illness (over 10 years). While no significant differences emerged for the epilepsy group, increased ventricular size with longer duration was present in the neurological group \( (P < 0.05) \). Individual t tests, however, were significant only for the difference between the 0 to 2 year group versus the over 10 year group. Symmetry scores did not differ significantly for any of the groups.

Table IV summarizes the ventricular measurements as a function of neurological examination results. No significant difference in mean ventricular size was apparent, comparing the group with abnormal examination results with either the non-neurological subjects only, or with patients from the epilepsy and neurological groups with normal examinations, or with all subjects from any group with normal neurological examination. While all subjects were rank ordered by ventricular size, a trend was present for more subjects with abnormal examination results to be present in the upper and middle thirds of the ventricular size distribution. However, the subject with the largest ventricles as well as the third, sixth, and eighth subjects in the rank order had normal neurological examinations; also, the subject with the next to smallest ventricular size had an abnormal examination.

Of particular interest was the failure to demonstrate differences in mean symmetry scores for the subjects with lateralized abnormalities on physical neurological examination as opposed to subjects with normal examination, or with bilateral abnormal findings. To illustrate this, Table V lists the rank order symmetry scores for all subjects with 80% symmetry or less, and the summary of examination findings in each patient.

Table V shows that only four of 23 patients had examination findings which were clearly contralateral to the larger ventricle. Thirteen patients in the same sample had physical examination summaries described as either 'within normal limits' or 'non-lateralizing', and five patients showed definite bilateral findings. Examination findings ipsilateral to the enlarged ventricle were recorded for one patient.
Three different linear measures were made in subsamples of varying size to permit correlation between the linear measurements and planographic data. The septal-caudate line ranged from 0.7 to 3.8 cm with a mean of 1.6 cm. The greatest transverse diameter of the cella media ranged from 1.3 to 3.3, with a mean of 1.9 cm. The ventricular span ranged from 2.0 to 6.6 cm with a mean of 4.3 cm. These results are comparable with those reported by other investigators using the same measures (Engeset and Skraastad, 1964).

For the septal-caudate line and the greatest transverse diameter, a correlation was computed from these measures and from the planographic scores for individual ventricles. Because the ventricular span measurement reflects the combined size of the two lateral ventricles, the correlation was based upon this linear score and the measure of combined planographic ventricular size. For each comparison the planographic and linear measurements for the same subjects were rank ordered from largest to smallest and a Spearman rank order correlation was computed. The strength of association between the rank orders was least for the greatest transverse diameter (Rho = 0.72). The highest correlation was obtained with the septal-caudate line (Rho = 0.97) followed closely by the ventricular span (Rho = 0.93).

Since the transverse diameter and the septal-caudate line measures are based upon individual ventricles, symmetry ratios could be expressed for these measurements. These ratios therefore can be compared directly with the symmetry ratios obtained from the planographic measurements on the same subjects. Again, the correlation was greatest for the septal-caudate line \( r = 0.83 \) and least with the transverse diameter \( r = 0.50 \).

**DISCUSSION**

Most investigators have agreed that the anterior portion of the body of the lateral ventricle at the level of the foramen of Monro is the best single area for measurement. This area, the cella media, represents the body of the familiar butterfly pattern seen on the brow-up anterior-posterior PEG film (Fig. 2). Knudsen (1958), using necropsy material, reported that linear measures correlated poorly with the volume of the ventricular system, but that the septal-caudate line, from the superior medial angle of the cella media to the most medial projection of the caudate nucleus, gave the highest correlation. Basing his conclusion upon a carefully quantified study of PEG measurements, Bruijn (1959) states that a linear measure of the cella media was a better measure of the size of the lateral ventricle than any of several other measures or ratios. In the present study, a rank order correlation between the septal-caudate line and planographic measures was extremely high (Rho = 0.97).

The only recent study to employ an area rather than a linear measure for clinical correlation...
utilized a ratio of the area of the lateral ventricle to the area of the skull as seen in lateral projections (Kiev et al., 1962). Selby (1968) was able to correct for magnification factors and reported planimeter measures of the cella media ranging from 0·8 cm² to 7·1 cm² in subjects with Parkinsonism. Our results are uncorrected for magnification but are in general agreement with Selby’s results. However we observed a much higher upper range of 10·7 cm². In addition, he used linear measures for clinical correlation. In both studies, measurement of the area of the cella media was facilitated by the use of the planimeter.

The results presented on the average error of measurement in the control studies described in the section Radiographic Methods were based upon any difference between first and second measurement, without regard for direction of change. When the direction of change between the two measurements was considered, the average error for all three control studies was less than 3%, indicating that planographic measurements are reliable. The data from the 12 individuals in whom repeat PEGs were available suggest that, once the cella media is adequately visualized, it is not likely to be significantly changed in size or configuration by differences in the amount of air injected or by other minor changes in technique. Support for this finding is provided by Robertson (1957) who has stated that adding more gas had the effect of filling the ventricles progressively backwards when brow-up films are taken but that this procedure does not change the size or shape of the ventricle. A similar conclusion was reached by Davies and Falconer (1943), who found no difference in linear measures of the cella media in four subjects in whom serial measurements were obtained following the injection of increasing amounts of air. Haug (1962), in a study of institutionalized psychiatric patients, measured repeat pneumoencephalograms in 31 subjects. The interval ranged from three months to 4½ years with a mean of 2½ years. In 15 cases all of the measures were the same. In 11 cases, there were minor differences which the author considered insignificant. In only five instances was a substantial increase noted in the size of the ventricles.

The increase in size of the lateral ventricles as a function of age in the present study was consistent with previous reports, as was the finding that the greatest increase occurred in the older age groups. However, the degree of asymmetry of the lateral ventricles was not related to age in the subjects studied here.

The most striking finding in our series was the significant increase in total ventricular size in the neurological as compared with the epilepsy and non-neurological groups. No difference in ventricular size between the epilepsy and non-neurological groups was apparent. Subjects with epilepsy, but with a more primary neurological diagnosis, of which the seizures were considered a symptom, were assigned to the primary neurological group. Although the mean age of the neurological group was slightly higher than for either of the other two groups, the difference is not sufficient to explain the differences in ventricular sizes.

While the number of patients in each duration classification was small, a significant increase in ventricular size between the shortest and longest duration of illness groups was seen for the neurological group. No comparable difference was apparent in the epilepsy group nor did symmetry results differ for either group. Had the numbers in each group been higher, perhaps more significant results would have been obtained. Nevertheless, several subjects in the epilepsy group had intractable seizures for 10 to 20 years. The findings suggest that seizures themselves, in the absence of a definable primary neurological disease, are not associated with enlargement of the lateral ventricles. Size and symmetry results for the generalized and focal groups within the epilepsy group were analysed separately but no significant differences were seen.

A similar result was reported by Larsby and Lindgren (1940), who found only a trend for increased ventricular size with increased duration of seizures in a study of 125 institutionalized epileptics.

The findings on symmetry measures in the variously composed groups tend to parallel the results of ventricular size. Significantly greater asymmetry was found in the neurological group than in the non-neurological subjects. The mean score for the epilepsy group was midway between the other two and did not differ significantly from either. Some degree of asymmetry of the lateral ventricles has been a constant finding in all studies in which the lateral ventricles have been measured. Symmetry scores in the present study ranged from 30 to 100% with a mean of 85%. One-fourth of the present sample had ventricular measurements which were considered symmetrical (96 to 100% symmetry), while approximately one-third showed mild asymmetry (95 to 86%). The remaining one-third (37%) had symmetry ratios below the group mean of 85%. Thirty-six of these 38 subjects were members of either the neurological or epilepsy groups, while only two were from the non-neurological group. Thus while some degree of asymmetry of the lateral ventricles is a common finding both in neurological and non-neurological patients, the largest asymmetries in our series were strongly associated with evidence of neurological disease. The relative enlargement of the left lateral ventricle reported in
previous studies was confirmed in the present investigation, and was present in a ratio of 2:1 for the non-neurological group. Typical of such findings is the difference reported in necropsy material by Knudsen (1958), in which he found the average volume of the left lateral ventricle to be greater than the right. In addition to these data on the ventricular system which suggest structural asymmetry of the hemispheres, Geschwind and Levitsky (1968) have recently reported asymmetries in the temporal speech region of the human brain.

A result of considerable interest in the present study was the absence of any demonstrable relationship between ventricular size or symmetry ratios and the results of the neurological examination. A similar poor clinical-radiological correlation has been reported for head injury (Davies and Falconer, 1943). While ventricular size correlated well with general incapacity and dementia in Parkinsonism (Selby, 1968) and Huntington's chorea (Gath and Vinje, 1968), a poor correlation was found for specific neurological deficits in both conditions. The absence of such a relationship is not surprising, since a small lesion, critically placed—for example, in the internal capsule—may have a profound effect upon the neurological examination status of the patient but need not contribute to enlargement of either lateral ventricle.

A higher correlation between PEG findings and neurological examination was reported by Hunter et al. (1962). However, their original pool of subjects was selected on the basis of a significant asymmetry in the PEG, and the subjects studied were further restricted to patients whom the authors considered to have abnormally large ventricles. In spite of these selection factors, only 60% of their subjects showed abnormalities on the neurological examination contralateral to the enlarged ventricle. Of the 75 subjects, six had abnormalities limited to the ipsilateral body side, and three had bilateral findings. Many subjects were considered to present only mild or transitory signs or symptoms. The authors felt that the failure to demonstrate a stronger relationship might be explained in part by the non-quantified nature of the neurological examination. As was the case in the present study, the patients investigated by Hunter et al. (1962) showed a variety of aetiological and clinical manifestations, and there was no specific clinical pattern associated with the unilaterally dilated ventricle.

While ventricular size and symmetry correlated with group classification in the present study, there was no correlation with the status on neurological examination of the individual patient. Since subjects were excluded if a tumour or other lesion which distorted the general topography of the ventricular system was present, all PEGs had been initially read by the radiologists of the respective institutions as either normal or showing only ventricular enlargement or asymmetry. A better correlation with clinical findings might be expected had subjects with such lesions been included. For instance, the focal dilatation of the lateral ventricle associated with a porencephalic cyst usually correlates with the neurological deficit. This exclusion was necessary, since a measure of any single portion of the ventricle—in the present case, the cella media—in the presence of a focal abnormality in some other portion, would not reflect the general size and symmetry features of the system. Under such conditions, comparison of individual subject findings by standard measures would be impossible unless a very large number of subjects could be surveyed. Thus the results reported can be related to clinical-neurological correlation only for subjects who show no focal distortion or mass lesion on the PEG.

**SUMMARY**

Planographic measurements of the area of the cella media as seen in anterior posterior projections of pneumoencephalograms were obtained in 104 subjects. Thirty-six subjects had epilepsy of unknown cause, 36 had more specific or primary neurological diagnoses, and 25 subjects were free from evidence of neurological disease or deficits. A positive relationship was found between increase in ventricular size and age for the total sample. Significantly larger lateral ventricles were found in the subjects with a primary neurological disease than in either of the other groups, but the epilepsy group did not differ from the non-neurological group in this regard. Ventricular size was related to duration of illness in the neurological group, but not in the epilepsy group. The findings on asymmetry of the lateral ventricles were less marked but tended to be parallel with those of ventricular size, in that 36 of 38 subjects with the greatest asymmetry ratios were from the primary neurological or epilepsy groups. Neither ventricular size nor degree of asymmetry was correlated with the results of the neurological examination.

Rank order correlations computed between planographic measures and linear measures (septal and the ventricular span) were highly significant, suggesting that these linear measures are as adequate as planographic measures for routine determinations of relative ventricular size. The results suggest that, while increase in size and asymmetry of the lateral ventricles is significantly associated with the presence of non-surgical neurological disease, there is little correlation between individual examination results and ventricular appearance.
Chronic epileptic seizures, in the absence of a definable primary cause, are not associated with ventricular enlargement. Analysis of the neuropsychological test data and ventricular measures obtained in the present study is in progress and will be reported in a subsequent paper.

REFERENCES


