Regional cerebral blood flow, white matter abnormalities, and cerebrospinal fluid hydrodynamics in patients with idiopathic adult hydrocephalus syndrome

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Abstract

Objectives—(1) to evaluate regional cerebral blood flow (rCBF) with single photon emission computed tomography and ^{99m}Tc -hexamethylpropyleneamine oxime in patients with the idiopathic adult hydrocephalus syndrome (IAHS); (2) to examine regional cerebral blood flow (rCBF), gait, and psychometric functions before and after CSF removal (CSF tap test); (3) to assess abnormalities in subcortical white matter by MRI.

Methods—Thirty one patients fulfilling the criteria for IAHS (according to history and clinical and neuroradiological examination) were studied. Quantified gait measurements, psychometric testing, and rCBF before and after removal of CSF were obtained. Pressure of CSF and CSF outflow conductance were investigated with a constant pressure infusion method. Brain MRI was used to quantify the severity of white matter lesions and periventricular hyperintensities.

In IAHS a widespread rCBF hypoperfusion pattern was depicted, with a caudal frontal and temporal grey matter and subcortical white matter reduction of rCBF as the dominant feature. Removal of CSF was not accompanied by a concomitant increase in rCBF. Significant white matter lesions were detected only in a minority of patients by MRI. An altered CSF hydrodynamic state with a higher CSF pressure and lower conductance was confirmed.

IAHS is characterised by an abnormal CSF hydrodynamic state, associated with a widespread rCBF reduction with preference for subcortical white matter and frontal-temporal cortical regions. Furthermore in most patients MRI did not show white matter changes suggestive of a coexistent subcortical arteriolosclerotic encephalopathy. At least in the idiopathic group of patients with AHS, measurements of rCBF before and after temporary relief of the CSF hydrodynamic disturbance will not provide additional information that would be helpful in the preoperative evaluation but is suggestive of a preserved autoregulation of rCBF.

Keywords: hydrocephalus; regional cerebral blood flow; cerebrospinal fluid hydrodynamics; subcortical white matter

The syndrome of “normal” pressure hydrocephalus was first described by Hakim and Adams¹ and Adams *et al.*² In our opinion the adult hydrocephalus syndrome (AHS) is a more appropriate description for the condition.^{3,4} The cardinal clinical features are disturbance of gait and balance often associated with a cognitive decline and an impaired control of sphincters due to chronic hydrocephalus. Permanent drainage of CSF has the potential to relieve symptoms.

There have been many suggestions of ancillary tests to select appropriate candidates for a shunt.^{5,6} The clinical effect of CSF taps is widely used.⁷ The CSF tap test involves removal of 40–50 ml CSF. Any improvements of gait and cognition are registered. A good correlation between outcome of the CSF tap test and response to shunt operation has previously been described,^{8,9} but has not been reproduced by others.¹⁰ Changes in regional cerebral blood flow (rCBF) after CSF drainage have been reported but with conflicting results,^{11–14} probably explained by methodological dissimilarities and non-homogenous patient populations. Table 1 summarises the methodology and results. Except for one study,¹⁵ all investigators applied non-tomographic CBF methods without concomitant clinical assessment.

The relative flow pattern obtained by ^{99m}Tc -hexamethylpropyleneamine oxime (^{99m}Tc -HMPAO) correlates well with that measured by xenon-133¹⁶ and by ^{15}O PET.¹⁷ There are only a few previous rCBF studies using single photon emission computed tomography (SPECT) in AHS,^{6,18} and in particular SPECT with ^{99m}Tc -HMPAO.^{19,20}

The aim of this study was to investigate rCBF using SPECT with ^{99m}Tc -HMPAO in the diagnosis of patients with IAHS. Furthermore, the effects of CSF drainage on cortical and subcortical rCBF and clinical variables were analysed. Drainage of CSF was performed in the setting of a CSF hydrodynamic investigation to define basic CSF hydrodynamic characteristics, such as CSF pressure and conductance to CSF outflow. Subcortical white matter in particular was evaluated by means of MRI as abnormalities in white matter have been suggested to

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Table 1 Review of all adult hydrocephalus syndrome and CBF studies before and after CSF drainage

Authors and year	Method used	No of patients Total/ Idiopathic	Clinical testing before and after CSF drainage	Baseline CBF	Time of CBF measurement after CSF drainage	Increased CBF after CSF drainage
Matthew <i>et al</i> 1975 ¹¹	Xenon – 133 intracarotid injection. Non-tomographic	15/5	No	Decreased	Immediately	Yes
Grubbet <i>et al</i> 1977 ¹²	Intracarotid injection of several isotopes. Non-tomographic	6/6	No	Decreased	Immediately	Yes
Kushner <i>et al</i> 1984 ¹³	Xenon – 133 inhalation. Non-tomographic	19/11	No	Decreased	Within 30 min	No
Mamo <i>et al</i> 1985 ¹⁴	Xenon – 133 inhalation. Non-tomographic	25/18	No	Decreased	3 h	Yes
Moretti <i>et al</i> 1988 ¹⁵	¹²³ I-IAMP iv Tomographic	27/12	Not specified	Decreased	30 min	Yes
Kristensen <i>et al</i> (present study)	⁹⁹ Tc-HMPAO iv Tomographic	31/31	Yes	Decreased	3 h	No

iv = intravenous.

play a pathogenetic part in the development of hydrocephalus.²¹

Methods

INCLUSION

A prospective study of IAHS has been carried out at the Department of Neurology, University Hospital of Ume since 1988. The diagnosis was based on: (1) a gait disturbance as a predominant and obligate symptom; (2) mental impairment or urinary incontinence, or both (ranging from not clinically present to severe disturbances); (3) CT showing dilatation of the lateral ventricles but without severe cortical atrophy; (4) absence of another disease which might explain the clinical symptoms or radiological findings.

In selected cases MRI or EMG were conducted to exclude coexisting myelopathy, infratentorial abnormality, or neuropathy.

ANCILLARY INVESTIGATIONS

Clinical characteristics of the patients were assessed by a neurological evaluation and careful history (obtained from both the patient and a relative), CT, EEG, ECG, mini mental state examination,²² full blood cell count, erythrocyte sedimentation rate, serum electrolytes, tests of hepatic, renal, and thyroid function, blood glucose, syphilis and Borrelia serology, protein electrophoresis, B12/folic acid, and CSF protein and cell count.

CLINICAL DATA

For the purpose of this study 31 patients (22 men and nine women, mean age (SD) 71.6 (4.9) years) were included. None of the patients had an obvious precipitating cause such as subarachnoid haemorrhage, meningitis, or neurosurgery. All patients were therefore considered to be of idiopathic type, although the symptoms appeared in one patient after a minor cranial trauma. History included medically treated hypertension (16 patients); diabetes mellitus (five); and ischaemic heart disease (seven). No cerebrovascular incidents or history of alcoholic misuse were recorded.

The mean lateral ventricular index²³ measured by CT was 0.37 (range 0.30–0.49). Cortical atrophy was measured by visual rating

of the width of the sylvian fissure and the cortical sulci. Cortical atrophy was absent or slight in 25 patients and moderate in seven. The gait disturbance preceded the development of other symptoms in all but two patients. Gait was characterised by difficulty in initiating walking (“magnetic phenomenon”), postural instability, and shuffling. At the time of inclusion the following symptoms were present: gait disturbance alone (seven patients); gait disturbance in combination with dementia (MMSE < 25 points) (seven patients); gait disturbance in combination with urinary incontinence (nine patients); gait disturbance in combination with dementia and incontinence (eight patients).

CONTROL SUBJECTS

Fourteen healthy volunteers (eight men and six women, mean age 72.2 (SD 3.8) years), served as controls for MRI and SPECT investigations (one volunteer was investigated with SPECT but was not able to complete MRI investigation due to claustrophobia). All had normal neurological and laboratory examinations. Detailed neuropsychological testing documented an average level of function.

Informed consent was obtained from all patients and control subjects according to institutional guidelines. The study protocol was approved by the hospital ethics committee.

SPECT

The patients and volunteers were examined in a supine position with eyes open and ears unplugged in a quiet normally illuminated room. The HMPAO freeze dried kit (Ceretek, Amersham International, London, UK) was mixed with pertechnate ^{99m}Tc solution. Shortly after reconstitution and 15–45 minutes before data acquisition a dose of 550 mBq was injected intravenously. Silence was maintained for five minutes after injection. The head was immobilised to minimise movement artefacts. The orbitomeatal line was positioned vertically.

A single head rotating gamma camera (General Electric 400 T) equipped with a general purpose low energy collimator was used for imaging and a DEC PDP 11 computer sys-

tem for processing. During a 360 rotation 64 views of 20 seconds duration were acquired from each hemisphere in transverse slices. The tilt angle of the transaxial slices was corrected to the orbitomeatal line. The resolution of the imaging system has been measured to be 15 mm full width of half maximum in the plane of the reconstructed transverse sections.

QUANTITATIVE ANALYSIS

a standard CT brain atlas for reference to neuroanatomical structures²⁴ was used to guide the construction of a reference set of symmetric cortical and subcortical rectangular regions of interest for each of four adjacent orbitomeatal slices (1 pixel thick each). One of these corresponded to the cerebellum centred 1 cm above the OM line (OM1). In the supratentorial regions the orbitomeatal slices were respectively 3, 5, and 6 cm (OM3, OM5, OM6) above the orbitomeatal line.

Regional radioactivity count densities were obtained for a total of 12 pairs of bilaterally symmetric regions of interest. These were drawn as symmetrically as possible on the cerebellar hemispheres, at the cortical ribbon (frontotemporal and occipital grey matter on OM3, frontal and temporal and frontal and parietal grey matter on OM5 and OM6 respectively), and regions centred over subcortical structures (in the caudate nucleus on OM3, central white matter on OM5, and in the frontal and parietal white matter on OM6).

The cerebellar hemisphere with the highest count rate was used as the reference region. The cerebellum was chosen because AHS is not known to be associated with structural abnormalities in the cerebellum and mean rCBF in the cerebellum has been shown to be no different from normal controls measured with the xenon-133 method.¹⁹

A semiquantitative assessment of regional cerebral perfusion comparing cortical/subcortical to cerebellar regions of interest was expressed as a ratio between activity in each region of interest and the highest mean counting rate over one cerebellar hemisphere.

All subjects were examined once. In the patients with AHS a second cerebral perfusion study was carried out after the CSF hydrodynamic investigation.

Regions of interest were analysed by an investigator who was unaware of the clinical findings and with no knowledge of whether the SPECT investigations were before or after CSF removal.

MAGNETIC RESONANCE IMAGING

All MRI was evaluated by a senior neuroradiologist, unaware of the clinical findings as well of the results of the SPECT.

An MRI scanner with an ultra low field equipment working at 0.04 Tesla was used. (Acutscan, Instrumentarium, Helsinki, Finland). T1 weighted transaxial images were obtained as inversion recovery sequences (TR/TI/TE 1000/300/40 ms) and T2 weighted transaxial images as spin echo sequences (TR/TE 2000/150 or 2600/130

ms); 10 mm contiguous sections were used for evaluation; the slice thickness was 10 mm.

Abnormal areas of hyperintensities in the T2 weighted scan were defined as white matter lesions if they were ill defined, patchy, diffuse, localised in white matter only, and separate from the ventricles. Periventricular hyperintensities referred to areas of heightened intensity at the margins of the lateral ventricles.

To quantify severity of white matter lesions and periventricular hyperintensities a 0–3 scale was used: 0 = no visible hyperintensities; 1 = caps at the ventricular angles with thin or thick ventricular lining; 2 = white matter foci; 3 = irregular confluent white matter lesions. All evaluations were performed on the T2 weighted images and inversion recovery images were used mainly to confirm the decisions. A ventricular index similar to that used for CT was calculated.

CSF HYDRODYNAMIC INVESTIGATION

The CSF hydrodynamic investigation was performed according to the method described by Ekstedt²⁵ and presented in recent clinical studies.^{26 27}

The CSF pressure (Pcl) and the conductance of the CSF outflow pathways (Gop) were determined. At the end of the investigation a CSF tap was performed by lowering the CSF pressure to a value of about 0 kPa, corresponding to the removal of 30–40 ml of CSF.

The normal values for CSF hydrodynamic variables have been published elsewhere.³ The 30 oldest subjects in this material were selected (mean age (SD) 70.5 (4.8) years) to obtain a normal control material similar in age to the patients with AHS.

CSF TAP TEST

A comprehensive battery of tests was given the day before CSF hydrodynamic investigation (day 1) and at the same hour on day 2, three to four hours after CSF pressure lowering. The second SPECT investigation was performed on day 2 three to four hours after ICP lowering and at least 24 hours after the previous baseline SPECT investigation.

The battery included assessment of gait, cognitive function, and psychomotor speed.

Walking test

Gait was assessed by means of a standardised procedure. The subject was asked to walk 25 metres. The task was repeated three times and the mean gait velocity (m/s) and number of steps were calculated.

Psychological tests

Bingley's memory test,²⁸ a digit span test,^{20 29} and a peg board test³⁰ were given according to standard procedures.

Statistical methods

For comparisons between groups (controls and patients with AHS) and between clinical subgroups of patients with AHS, repeated measures analysis of variance (ANOVA) was employed. When necessary, post hoc compar-

isons were conducted with the Dunn-Sidak modification of the least significant difference test.³¹ Analyses of correlations between clinical variables and rCBF were conducted using Pearson's product-moment correlation coefficient. An α value smaller than 0.01 was considered significant.

Results

rCBF PATTERNS IN PATIENTS WITH LAHS

Figures 1A–C (grey matter) and fig 2 (white matter) show the results pertaining to differences between controls and patients with AHS.

A separate $2 \times 2 \times 2$ (group by cortical region by hemisphere) ANOVA was performed for slices OM6 and OM6 depicting grey matter perfusion. In OM6 (fig 1A), there were no significant effects.

In OM5 (fig 1B) regions of interest, the ANOVA disclosed a marginally significant effect of group ($F(1,41) = 5.01$; error mean square (MSe) = 0.017; $P < 0.03$). Because the group factor did not enter any significant higher order interaction, this result means that patients with AHS showed hypoperfusion with regard to all regions of interest. Besides the putative difference between the two groups, there were no other statistically significant effects.

A $2 \times 3 \times 2$ (group by cortical region by hemisphere) ANOVA was conducted to analyse the results in OM3 grey matter regions

Figure 1 A–C rCBF (expressed as cerebral/cerebellar ratios) for cortical grey matter. See text for further explanations; ROI = region of interest.

Figure 2 rCBF (expressed as cerebral/cerebellar ratios) for subcortical structures. See text for further explanations; ROI = region of interest.

of interest (fig 1C). There was a significant main effect of group ($F(1,40) = 10.56$; MSe = 0.02; $P < 0.01$). In addition, the effect of cortical region was statistically significant: $F(2,80) = 45.92$; MSe = 0.005; $P < 0.01$. No other effect was statistically significant. Post hoc testing showed that all regions of interest differed; occipital regions of interest showing higher perfusion than temporal regions of interest. The last in turn showed higher perfusion than frontal regions of interest. In conclusion, parietal and upper frontal grey matter rCBF of patients with AHS were relatively preserved, whereas a pronounced hypoperfusion corresponding to inferior frontal and temporal cortex was evident. Patients with AHS as well as controls showed lower perfusion in anterior than in posterior regions of interest.

Figure 2 presents the results for subcortical structures. In OM6, a $2 \times 2 \times 2$ (group by white matter region by hemisphere) ANOVA (the term "white matter region" depicting frontal and parietal white matter respectively) was performed. The main effect of group was significant ($F(1,40) = 22.28$; MSe = 0.04; $P < 0.01$). Apparently, there was a pronounced decrease in rCBF corresponding to frontal and parietal white matter in the patients with AHS. In OM5 and OM3, significant main effects of group were obtained ($F(1,41) = 633.02$; MSe = 0.0002; $P < 0.01$ and $F(1,40) = 20.8$; MSe = 0.002; $P < 0.01$).

CSF TAP TEST RESULTS

The effects of CSF tap on gait, motor speed, attention, and memory were evaluated by t test (table 2). An improvement was obtained with respect to the time based measure derived from the gait test—that is, the time needed to walk the designated route ($t(25) = 2.42$; $P < 0.05$). Effects on memory, digit span, and the peg board test were not significant.

To assess whether removal of CSF would improve cerebral perfusion, a series of six separate ANOVAs were carried out, one for each of the three slices and for grey and white matter respectively. In these analyses, CSF tap, regions of interest, and hemisphere served as factors. Although these analyses yielded effects of regions of interest, CSF tap did not produce any significant effect.

Table 2 Mean effects of removal of CSF (CSF tap test) on selected clinical and neuropsychological measures in patients with IAHS

Test	Before tap	After tap
Memory (items)	3.16 (0.40)	3.14 (0.38)
Digit span (items)	2.44 (0.33)	2.67 (0.36)
Walking test (No of steps)	70.65 (12.38)	50.08 (8.49)
Walking test (duration in s)	61.62 (12.68)	37.73 (7.83)
Peg board test(s)	92.92 (6.82)	90.42 (7.58)

Values in parenthesis are SEM.

CORRELATIONS BETWEEN rCBF BEFORE AND AFTER CSF TAP AND CLINICAL CHANGES

A main concern of this study was to determine whether changes in rCBF parallel clinical changes in gait and memory. To clarify this, a series of correlations (Pearson's *r*) between rCBF at different regions of interest and measurements of gait, memory, motor speed, and attention were carried out. There were no significant correlations between changes in rCBF and clinical change in the AHS group (all *P* values > 0.10). Table 3 shows the results for grey matter regions of interest.

CSF HYDRODYNAMICS

Pressure of CSF was moderately increased in the IAHS group. The mean for the patients with IAHS was 1.8 kPa (95% confidence interval (95% CI) 1.6–2.0 kPa and that for healthy controls was 1.3 kPa (95% CI 1.2–1.4 kPa). Furthermore, the conductance was low in IAHS (8.9 (95% CI 7.6–10.3) mm³/kPa/s). The corresponding value in control subjects was 17.4 (95% CI 16.0–18.8) mm³/kPa/s.

NEURORADIOLOGICAL FINDINGS

The mean lateral ventricular index was 0.40 (range 0.33–0.49) for MRI in the IAHS group and for controls it was 0.20 (range 0.16–0.30). To exclude patients with possible obstructive hydrocephalus, evaluation of MRI investigations was also directed against signs of aqueductal stenosis; no such patients were identified.

Table 4 describes the white matter lesions in the AHS and control groups. The rating of all white matter lesions disclosed a tendency towards increased prevalence of MRI abnormalities in AHS (70% *v* 38%; $\chi^2(1) = 3.77$; *P* < 0.10). The prevalence of moderate and severe white matter lesions showed a signifi-

Table 4 Frequency of lesions of the cerebral white matter (WML) in the IAHS and control groups, graded on a four point scale

WML (grade)	Controls (n = 13)	IAHS (n = 30)
0	8	9
1	4	7
2	0	6
3	1	8

cant difference ($\chi^2(1) = 8.3$; *P* < 0.01).

Findings from MRI were compared with rCBF to clarify if there was a relation between abnormalities in white matter and rCBF. Association between white matter lesions and rCBF was analysed by means of four different ANOVAs. There were no significant main or interaction effects (all *P* values > 0.10).

Discussion

The clinical events during CSF tap tests have only been systematically evaluated in a few studies,^{8,32,33} and with no comparative rCBF measurements. Removal of CSF induced gait improvement in the present study, but did not alter the performance on cognitive tasks. There was no correlation between improvement of gait and rCBF, or any detectable rise in rCBF after CSF removal. Hence, rCBF investigation before and after CSF drainage does not provide additional information or guidance in the preoperative evaluation of patients with IAHS with respect to decisions regarding shunt operation. In one previous study, the amount of CBF increase after CSF removal was related to clinical improvement after shunting,¹¹ but this finding has not been reproduced by others.¹⁴ Changes in rCBF after CSF drainage have been explained as being the result of impaired autoregulation¹¹ or due to a mechanical phenomenon originating through a decrease in intraparenchymal pressure after the drainage.¹⁴ Studies of cerebral haemodynamics in patients with AHS have shown conflicting results^{11–13,34} but autoregulation has been reported to be maintained in IAHS.³⁵ According to the present study, autoregulatory properties of the cerebral circulation with respect to variations in CSF pressure are preserved.

Studies of rCBF with SPECT in patients with AHS have all shown decreased rCBF. However, the areas of impaired flow differ from study to study, ranging from global hypoperfusion⁶ to predominantly reduction in the frontal area.¹⁵ Several PET studies have shown cortical hypometabolism in the whole brain and depressed cerebral metabolism in conjunction with a decrease in rCBF^{36–38} or impairment of cerebral oxygen metabolism in the cerebral cortex of the caudal regions of the brain, particularly in the frontal lobes.³⁸

In this study a widespread cortical hypoperfusion pattern was obtained in IAHS. Large deficits were noted with respect to caudal frontal and temporal grey matter and in subcortical white matter. A modest reduction was seen in specific subcortical nuclei. A similar pattern of rCBF disturbances obtained with

Table 3 Pearson correlation coefficients depicting relations between changes in rCBF, regions of interest in grey matter, and changes in performance on clinical tests after CSF drainage

	Memory	Digit span	No of steps	Speed of walking	Peg board
OM6PL	-0.383	-0.207	0.203	0.234	-0.188
OM6PR	-0.265	0.080	0.243	0.215	-0.061
OM6FL	-0.235	-0.041	0.017	0.093	0.015
OM6FR	-0.256	-0.073	0.136	0.145	-0.088
OM5TL	-0.060	-0.015	0.063	0.114	-0.084
OM5TR	-0.019	0.151	0.058	0.103	-0.052
OM5FL	-0.253	0.028	-0.087	-0.020	-0.157
OM5FR	-0.300	-0.050	0.151	0.143	-0.265
OM3OL	0.162	-0.090	0.031	0.129	-0.020
OM3OR	-0.030	0.169	0.194	0.088	-0.065
OM3TL	0.045	0.024	-0.311	-0.102	0.050
OM3TR	-0.167	0.077	-0.150	-0.056	0.053
OM3FL	-0.304	0.093	0.237	0.162	-0.254
OM3FR	-0.262	0.008	0.106	0.020	-0.464

P* < 0.05; *P* < 0.01 with Bonferroni correction.

F = frontal; T = temporal; P = parietal; O = occipital; R = right; L = left.

the ^{99m}Tc -HMPAO method was found in two recent studies. In addition to an enlarged subcortical low flow region, Waldemar *et al*¹⁹ studied 14 patients with AHS (11 IAHS) and found a relative reduction of blood flow in the frontal and temporal cortex and in the central white matter. In the study of Larsson *et al*²⁰ rCBF measurements derived from 23 patients with AHS (11 IAHS) showed decreased rCBF in the temporal (hippocampal) regions and in the frontal and parietal white matter. However, these studies did not report their findings separately for IAHS and secondary forms of AHS. Hence, the present study represents the first major description of rCBF in IAHS. Cerebral blood flow changes related to outcome of shunt operation is not considered in this study, but no good relation has been established between baseline CBF and outcome after CSF diversion.³⁹

The sensitivity for detection of white matter lesions with low field strength MRI and high field strength MRI is probably equivalent.⁴⁰ There was a tendency (non-significant) for white matter lesions on T2 weighted MRI to be more common in patients with IAHS than in controls. A few patients with IAHS had more extensive lesions. Bradley *et al*²¹ reported similar findings in their MRI study of 20 patients with presumed AHS. In their study only three patients had severe and confluent deep white matter lesions although inclusion criteria were not detailed. In the presence of impaired CSF hydrodynamics characterised by a moderate increase in CSF pressure and a low conductance, even small changes in CSF pressure may have an adverse effect, giving rise to ischaemia of the periventricular white matter. Potential mechanisms of white matter change, ischaemia of the periventricular white matter, and depression of nerve cell function secondary to hydrocephalus may include periventricular diffusion of CSF and an increase in intraparenchymal pressure. The reduction of rCBF in grey matter may be a secondary phenomenon to decreased blood flow in the subcortical white matter reflecting a functional disconnection of cortical regions from deeper brain structures.

The predetermined specified clinical and neuroradiological criteria applied in this study are in accordance with the criteria proposed for "probable shunt responsive" patients with AHS.⁴¹ Combined rCBF, CSF hydrodynamic, and MRI data for the particular group of patients with IAHS have not been presented before.

To summarise, the following characteristics emerged: (1) an rCBF pattern clearly different from the normal aging brain; (2) an abnormal CSF hydrodynamic profile; (3) for most patients white matter lesions were not a prominent feature. In our experience a shunting procedure improves the clinical status in 70% of patients with IAHS as defined in this study.¹⁰

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NEUROLOGY IN LITERATURE

Some of Trollope's doctors

Trollope has a rather gentler view of the medical profession than Dickens, although Dr Fillgrave receives some adverse comment and, predictably, comes off worse in a clash with Dr Thorne. Many of Trollope's comments still seem apposite. Doctors still love their fees, remain bad actors, and perhaps are still a potential hazard in the houses of young ladies!

Anthony Trollope, 1857, Barchester Towers

No change, gentlemen; not the slightest change—but a telegraphic message has arrived—Sir Omicron Pie will be here by the 9-15 pm train. If any man can do anything Sir Omicron Pie will do it. But all that skill can do has been done.

Anthony Trollope, 1858, Doctor Thorne

Now Dr Fillgrave dearly loved a five-pound fee. What physician is so unnatural as not to love it? He dearly loved a five-pound fee; but he loved his dignity better.

Anthony Trollope, 1858, Doctor Thorne

He was brusque, authoritative, given to contradiction, rough though never dirty in his personal belongings, and inclined to indulge in a sort of quiet raillery, which sometimes was not thoroughly understood. People did not always know whether he was laughing at them or with them; and some people were, perhaps, inclined to think that a doctor should not laugh at all when called in to act doctorially. . . .

To trifling ailments he was too often brusque. Seeing that he accepted money for the cure of such, he should we may say, have cured them without an offensive manner. So far he is without defence. But to real suffering no one found him brusque; no patient lying painfully on a bed of sickness ever thought him rough.

Anthony Trollope, 1864, The Small House at Allington
Young unmarried doctors ought perhaps to be excluded from houses in which there are young ladies. I know, at any rate, that many sage matrons hold very strongly to that opinion, thinking, no doubt, that doc-

tors ought to get themselves married before they venture to begin working for a living.

Anthony Trollope, 1864-5, Can you forgive her

But oh, Alice, if you had seen the Duke's long face through those three days; if you had heard the tones of the people's voices as they whispered about me; if you had encountered the oppressive cheerfulness of those two London doctors,—doctors are such bad actors,—you would have thought it impossible for any woman to live throughout.

Anthony Trollope, 1867, The last chronicle of Barset

Now Dr Fillgrave was the leading physician of Barchester, and nobody of note in the city—for the matter of that in the eastern division of the county—was allowed to start upon the last great journey without some assistance from him as the hour of going drew nigh. I do not know that he had much reputation for prolonging life, but he was supposed to add a grace to the hour of departure. . . .

"A day or two will see the end of it, Mr Archdeacon—I should say a day or two," said the doctor, as he met Dr Grantly in the hall. "I should say that a day or two will see the end of it. Indeed I will not undertake that twenty-four hours may not see the close of his earthly troubles. He has no suffering, no pain, no disturbing cause. Nature simply retired to rest." Dr Fillgrave, as he said this, made a slow falling motion with his hands, which alone on various occasions had been thought to be worth all the money paid for his attendance.

Anthony Trollope, 1870, The vicar of Bullhampton

She would not absolutely say that a physician was not a gentleman, or even a surgeon; but she would never allow to physic the same absolute privileges which, in her eyes, belonged to law and the church.

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