conditions) one by one at a rate of one stimulus per 5 s (stimulus presentation time=4 s, interstimulus interval=1 s). Stimuli were presented on a black background on a display controlled by a Windows computer.

List A (20 colored random shapes) was presented in one encoding condition (EC; encoding of colored shapes), and list B (20 white random shapes) in the other (EW; encoding of white shapes). During the two encoding conditions, subjects were asked to press a button with the index finger of their left hand as soon as the stimuli were presented and to memorize the shapes and colors of the stimuli. To boost subsequent retrieval, each encoding condition was repeated five times (from the second to the fifth runs: stimulus presentation time=3.5 s, interstimulus interval=0.5 s) and only the first encoding condition was scanned with PET.

List C (14 random shapes which were red or green at encoding, 3 random shapes which were white at encoding, and 3 new random shapes) was presented in one retrieval condition (RC; retrieval of colored shapes), and list D (14 random shapes which were white at encoding, 3 random shapes which were red or green at encoding, and 3 new random shapes) was presented in the other (RW; retrieval of white shapes). During an 80-s PET data acquisition, 14 shapes which were colored at encoding, 1 shape which was white at encoding, and 1 new shape were presented in RC, and 14 shapes which were white at encoding, 1 shape which was green at encoding, and 1 new shape were presented in RW. This procedure ensured that most of the activations occurring during the retrieval conditions were due to the target stimuli, i.e., white shapes which were colored at encoding in RC, and white shapes which were also white at encoding in RW. During the two retrieval conditions, subjects were asked to press one of four buttons with the fingers of their left hand: the index-finger button if they thought the stimulus had been presented in red at encoding, the middle-finger button if they thought it had been presented in green at encoding, the ring-finger button if they thought it had been presented in white at encoding, and the little-finger button if they thought it had not been presented at encoding.

Data acquisition

All the subjects' responses (and the reaction times) were recorded in a computer as they pressed the buttons, and these data were subsequently used for the evaluation of performance accuracy.

Regional cerebral blood flow (rCBF) was measured using PET (SET2400W Shimadzu, FWHM 4.0 mm) and ^{15}O-labeled water (approximately 180 MBq for each injection). The transaxial sampling field of view (FOV) was 256 mm, and the axial FOV was 190 mm. The thickness of the slices measured was 3.125 mm. Prior to the PET experiments, subjects had a catheter inserted into the right brachial vein for tracer administration, and their heads were fixed to an air-cushioned headrest apparatus. Each task started 10 s before PET data acquisition, and lasted 100 s. PET data acquisition lasted 80 s. A transmission scan was followed by the experiment, and the data were used to obtain corrected emission images. A T1-weighted MRI scan (1.5 T) was performed on a separate occasion for coregistration.

Data analysis

The data were analyzed with Statistical Parametric Mapping (SPM2) (Wellcome Department of Imaging Neuroscience, UK). All rCBF images acquired from each subject were realigned to correct for small movements occurring between scans. This process generated an aligned set of images and a mean image per subject. A T1-weighted structural MRI was coregistered to this mean PET image. Then the coregistered T1 image was normalized to the Montreal Neurological Institute (MNI) templates implemented in SPM2. The parameters from this normalization process were applied to each PET image. The PET images were reformatted to isometric voxels ($2\times2\times2$ mm^3) and smoothed with a Gaussian kernel of FWHM of 10 mm. The rCBF-equivalent measurements were adjusted to a global CBF mean of 50 ml/dl/min. Contrast of the condition effect of each voxel was assessed using *t*-statistics, resulting in a statistical image (SPMt transformed into an SPMz). In both standard pairwise contrasts (i.e., EC vs. EW and RC vs. RW) and a cognitive conjunction analysis (i.e., EC vs. EW conjunct with RC vs. RW) using the "global null" in SPM2 software (Friston et al., 1999, 2005), the threshold of significance was set at $p<0.001$ (uncorrected for multiple comparisons). It should be noted that our "significant conjunction" does not mean all the contrasts were individually significant (i.e., a conjunction of significance). It simply means that the contrasts were consistently high and jointly significant. This is equivalent to inferring that one or more effects were present. To reduce the possibility of false-positive results (Type 1 errors), we regarded clusters of 25 or more voxels as significant. The anatomical identification of activated regions was performed using a standard space of the Talairach and Tournoux (1988) through the transformation from MNI to Talairach space (Brett et al., 2002).

Results

Behavioral measures of task performance

The mean accuracy and reaction time were, respectively, 82.6% (SD=11.3) and 1760 ms (SD=322) for RC, and 76.8% (SD=20.3) and 1758 ms (SD=432) for RW. There were no significant differences (*t*-test) in either accuracy ($p=0.12$) or reaction time ($p=0.49$) (Fig. 2), suggesting that differences in brain activation between EC and EW and between RC and RW cannot be ascribed to a difference in task difficulty.

Brain activation

First, EC was compared with EW. This contrast showed brain activations in the bilateral occipital regions, left supramarginal

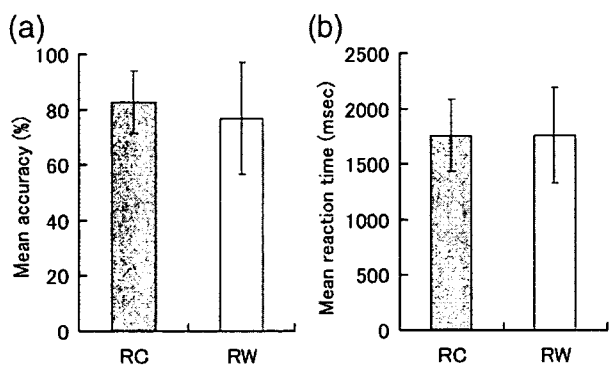

Fig. 2. (a) Mean accuracy of responses and (b) mean reaction times of the two retrieval tasks. Error bars indicate standard deviation. *T*-test showed no significant difference. Abbreviations as in Fig. 1.

Table 1
Brain regions showing activation in EC minus EW

Region (Brodmann's area)	MNI coordinates			Z value	Cluster size
	x	y	z		
R inferior occipital gyrus (BA18)	22	−94	10	4.14	114
L superior frontal gyrus (BA8/6)	−20	22	58	3.77	42
L putamen	−32	8	−4	3.87	34
L supramarginal gyrus (BA40)	−54	−56	46	3.95	26
L inferior occipital gyrus (BA18)	−14	−100	−4	4.37	136

EC, encoding of colored shapes condition; EW, encoding of white shapes condition; R, right; L, left.

gyrus, left superior frontal gyrus, and left putamen (Table 1 and Fig. 3a).

Second, RC was compared with RW. RC, relative to RW, was associated with activations in the right lingual gyrus and left middle occipital gyrus (Table 2 and Fig. 3b).

Finally, to determine whether brain regions activated during encoding were reactivated at retrieval, we used a conjunction analysis (EC vs. EW conjunct with RC vs. RW). This analysis revealed that the right parahippocampal gyrus, right lingual gyrus, right inferior occipital gyrus, and left putamen were active in both the encoding contrast and the retrieval contrast (Table 3 and Fig. 4).

Discussion

The results showed overlapping activity in the MTL and occipital lobe (the lingual and inferior occipital gyri) in the right hemisphere during the encoding and retrieval of meaningless shapes with color information compared with those without color information. In EC all stimuli were colored shapes, and in EW all stimuli were white shapes, whereas all of the stimuli in both of the retrieval conditions (RC and RW) were white shapes. Therefore, encoding-related activations in these regions probably reflect the on-line processing of color information from the external world (i.e., the process of actual color perception) and binding it with shapes. However, retrieval-related activity could not be attributed to the on-line processing of color information from the external world, but rather to the process of retrieval of color information from the recognized shapes. Hence, this finding seems to support the reactivation hypothesis that postulates that the retrieval of specific event information is associated with the reactivation of both the MTL structures and regions that were involved during the encoding of this information.

The overlapping activity found in the MTL during the encoding and retrieval of color information attached with shapes was consistent with the findings of the study by Nyberg et al. (2000), which focused directly on the reactivation of brain regions. Nyberg et al. found left MTL activation during both the encoding and retrieval of sound information paired with words, relative to words presented alone. The results of the present study are also compatible with those of studies of memory retrieval in the context of reactivation (Gottfried et al., 2004; Woodruff et al., 2005) cited in the Introduction. With regard to the successful encoding or retrieval of color information, three neuroimaging studies have demonstrated MTL activation, although overlapping activity between encoding and retrieval was not assessed. Yonelinas et al. (2001), using fMRI, reported that bilateral MTL structures were activated during an associative recognition task (clip-arts with colors) compared with a simple old/new judgment task. Ranganath et al. (2004) showed that activation of two right MTL regions (the posterior hippocampus and

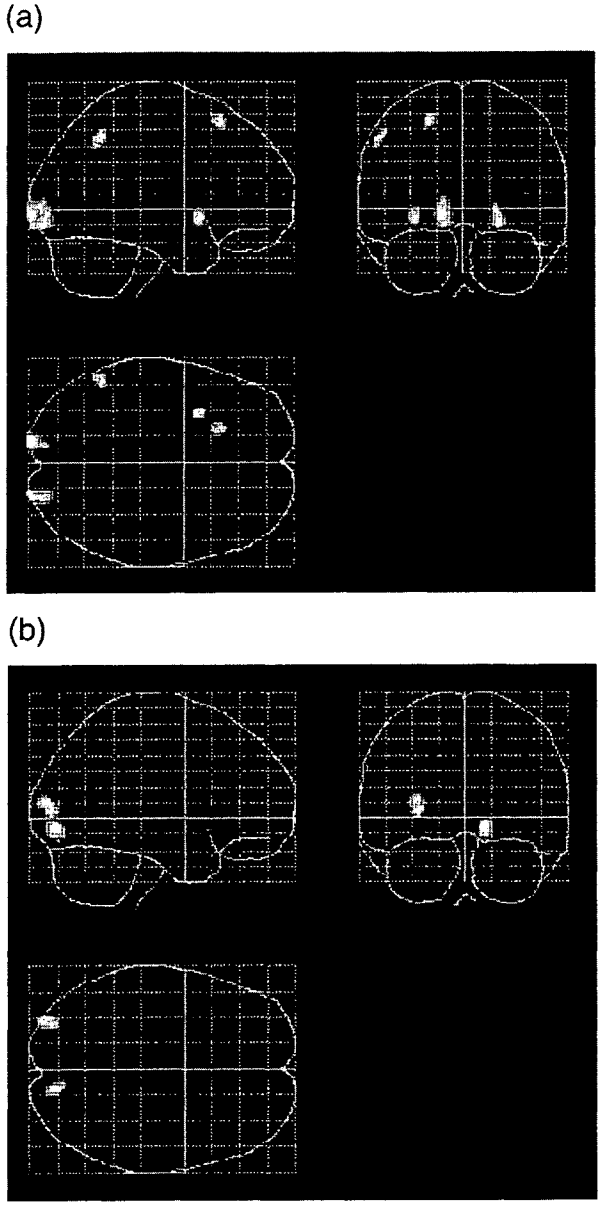

Fig. 3. (a) Brain regions showing activation in comparison of EC with EW. (b) Brain regions showing activation in comparison of RC with RW. The activations are superimposed onto MRIs of Montreal Neurological Institute (MNI) templates. Abbreviations as in Fig. 1.

Table 2
Brain regions showing activation in RC minus RW

Region (Brodmann's area)	MNI coordinates			Z value	Cluster size
	x	y	z		
R lingual gyrus (BA18)	14	−86	−6	4.02	69
L middle occipital gyrus (BA18)	−32	−90	10	3.73	72

RC, retrieval of colored shapes condition; RW, retrieval of white shapes condition; R, right; L, left.

Table 3
Brain regions showing overlapping activity during encoding and retrieval of color information

Region (Brodmann's area)	MNI coordinates			Z value	Cluster size
	x	y	z		
R parahippocampal gyrus (BA28)	18	−22	−16	3.68	25
R lingual gyrus (BA18)	18	−88	−6	4.12	83
R inferior occipital gyrus (BA18)	34	−88	−16	4.45	58
L putamen	−30	10	0	3.78	36

R, right; L, left.

posterior parahippocampal cortex) at encoding predicted subsequent successful retrieval of color information attached with words. Weis et al. (2004) found increased activity in bilateral MTL structures in successful color retrieval attached with buildings/landscapes at encoding. Collectively, the present findings and the data from these previous studies suggest that the MTL structures are engaged in binding specific event information with items during encoding and in recovering the same information from items during later retrieval.

Interestingly, overlapping MTL activity was identified in the right hemisphere in the present study. One possible reason for this is that the constituents of the materials encoded and retrieved in this study were non-verbal (the association between random shapes and colors). This explanation is consistent in part with some previous studies showing right MTL activation during memory for pictures and odors (Gottfried et al., 2004), bilateral MTL activation during the retrieval of colors from clip-arts (Yonelinas et al., 2001) and of colors from buildings/landscapes (Weis et al., 2004), and left MTL activation during memory for words and sounds (Nyberg et al., 2000). Two studies, however, have not reported right MTL activation during the successful encoding of words and colors (Ranganath et al., 2004) and during the retrieval of pictures from words (Woodruff et al., 2005). This may be related to the fact that these two studies found MTL activation in a somewhat different comparison (recollection-related activity; i.e., remember responses vs. know responses) from that used in others.

On the other hand, some studies have found no activation in the MTL in the context of reactivation (Nyberg et al., 2001; Persson and Nyberg, 2000; Vaidya et al., 2002; Wheeler et al., 2000). Persson and Nyberg (2000) and Wheeler et al. (2000) compared associative tasks with each other, a situation in which activation of the MTL might be cancelled out. Similarly, in the study by Nyberg et al. (2001), since the baseline condition was an associative learning task (rehearsing verb–noun commands), comparison between the target conditions (overt enactment and covert enactment) and the baseline condition might weaken the differences in activation of the MTL. Vaidya et al. (2002) compared recognition memory judgments related to words that were encoded as pictures with those that were encoded as words, and reported no activation in the MTL structures. However, their study did not involve any explicit associative learning, and it is possible that an associative learning procedure might be necessary to trigger MTL activation. The precise circumstances in which MTL activations are found (including, for example, combinations of constituents to be remembered, task procedures, and the method used for statistical comparisons) should be determined carefully in future studies.

The right occipital lobe (the lingual and inferior occipital gyri) also showed overlapping activity during the encoding and retrieval of color information attached with shapes. These sites are close to the color perception areas (V4; 28, −78, −14/−30, −76, −16) demonstrated by Bartels and Zeki (2000). Chao and Martin (1999) reported that the right lingual gyrus is associated with color perception. Moreover, Howard et al. (1998) showed that color perception activated the bilateral posterior fusiform gyri (area V4), as well as the right-sided anterior fusiform and lingual gyri, striate cortex (area V1), and bilateral insula. However, as mentioned above, whereas encoding-related activations could be attributed to the on-line processing of color information from the external world and the binding of color with shapes, this is not the case for retrieval-related activity, which is attributable to the processes of retrieval of color information from recognized shapes. Related to this, Miceli et al. (2001) reported two brain-damaged patients who exhibited an unusual pattern of object color knowledge loss but spared color perception and naming, suggesting that the brain regions subserving color retrieval and color perception are not the same. Therefore, the overlapping activity in the occipital lobe found in the present study probably reflects processes necessary for association between the color and shape of stimuli rather than processes of color perception itself.

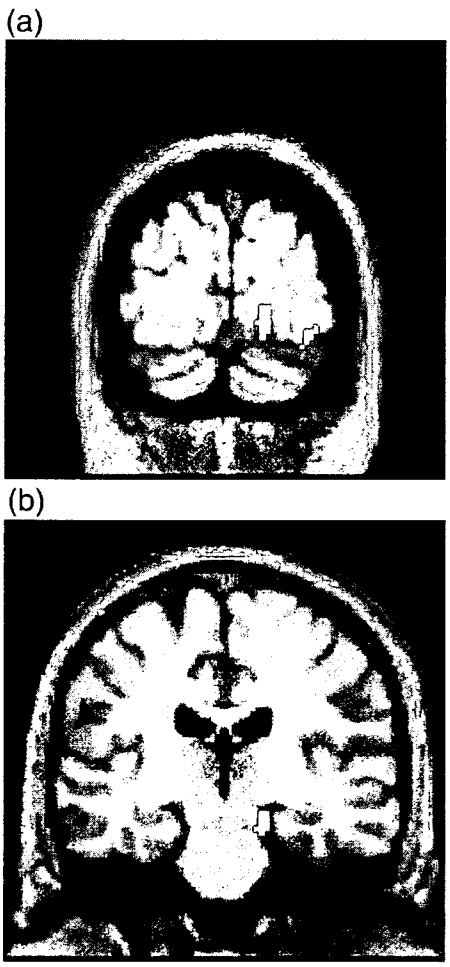

Fig. 4. Brain activations common to the encoding and retrieval of color information (EC vs. EW conjunct with RC vs. RW). The activations are superimposed onto MRIs of Montreal Neurological Institute (MNI) templates. (a) Right lingual gyrus (18, −88, −6), right inferior occipital gyrus (34, −88, −16). (b) Right parahippocampal gyrus (18, −22, −16). Abbreviations as in Fig. 1.

Other than our hypothesized regions, overlapping activation of the left putamen, one component of the basal ganglia, was found during the encoding and retrieval of color information attached with shapes. Although the basal ganglia are usually thought to have a role in regulating motor behavior, previous studies have clarified their role in language processing such as word fluency, sentence comprehension, and verbal long-term memory (D'Esposito and Alexander, 1995; Grossman, 1999; Risse et al., 1984). One possible interpretation is that the activation of the left putamen might be associated with an increased cognitive demand of language processing during EC and RC (relative to EW and RW), where subjects might inwardly generate two color names throughout the conditions.

Finally, it is necessary to mention the limitations of the present study. First, we used PET and a blocked design as a measure of brain activation. Compared with fMRI, PET has the advantage of detecting some regional activation (e.g., orbitofrontal cortex, anterior temporal lobe structures, and other regions showing magnetic susceptibility-induced signal losses due to the sinus cavities), but the blocked design raises issues of expectation or effects of selective attention on activation patterns. Second, the use of multiple encoding procedures makes the relevance of the present results to episodic memory or semantic memory uncertain. A similar criticism can be applied to other previous studies (Gottfried et al., 2004; Vaidya et al., 2002; Wheeler et al., 2000). To clarify this point, it might be useful to assess the difference in brain activation between a single-study procedure and a multiple-study procedure. Alternatively, in the present study, a remember/know procedure during retrieval could have been informative. Third, to achieve our goal, it might not be necessary to use two different colors (red or green) as specific event information attached with shapes. Encoding or retrieval, or both, of two different colors might be more demanding for cognitive processes than encoding and/or retrieval of a single color, and this might be a confounding factor in the interpretation of the data, although there were no significant differences in the behavioral measures between the two retrieval conditions (RC and RW). Finally, it is not clear whether activation in the MTL is preceded by activation in the occipital lobe or vice versa during the encoding and retrieval conditions. In order to prove the validity of the reactivation hypothesis, it is critical to determine the time course of activation in each region. The animal study conducted by Naya et al. (2001) showed that the memory-retrieval signal appeared earlier in the perirhinal cortex, and neurons in the inferior temporal cortex were then gradually recruited to represent the sought target. They suggested that this finding underlies the activation (reactivation) of neurons in the inferior temporal cortex that represent a visual object retrieved from long-term memory. Also, recent studies (Dhond et al., 2005; Masumoto et al., 2006) using magnetoencephalography (MEG) have reported the time course of activation patterns in some brain regions during a recognition test, although MEG does not easily detect signals in deep or medial brain structures. If the temporal resolution of non-invasive neuroimaging techniques such as event-related fMRI improves, it will be possible to determine the time course of activation patterns in several memory-related regions, including the MTL in the human brain.

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Increased colonic pain sensitivity in irritable bowel syndrome is the result of an increased tendency to report pain rather than increased neurosensory sensitivity

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NEUROGASTROENTEROLOGY

Increased colonic pain sensitivity in irritable bowel syndrome is the result of an increased tendency to report pain rather than increased neurosensory sensitivity

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Objective: The aim was to determine whether lower visceral pain thresholds in irritable bowel syndrome (IBS) primarily reflect physiological or psychological factors.
Methods: Firstly, 121 IBS patients and 28 controls underwent balloon distensions in the descending colon using the ascending methods of limits (AML) to assess pain and urge thresholds. Secondly, sensory decision theory analysis was used to separate physiological from psychological components of perception: neurosensory sensitivity (p(A)) was measured by the ability to discriminate between 30 mm Hg vs 34 mm Hg distensions; psychological influences were measured by the report criterion—that is, the overall tendency to report pain, indexed by the median intensity rating for all distensions, independent of intensity. Psychological symptoms were assessed using the Brief Symptom Inventory (BSI).
Results: IBS patients had lower AML pain thresholds (median: 28 mm Hg vs 40 mm Hg; $p<0.001$), but similar neurosensory sensitivity (median p(A): 0.5 vs 0.5; $p=0.69$; 42.6% vs 42.9% were able to discriminate between the stimuli better than chance) and a greater tendency to report pain (median report criterion: 4.0 ("mild" pain) vs 5.2 ("weak" pain); $p=0.003$). AML pain thresholds were not correlated with neurosensory sensitivity ($r=-0.13$; $p=0.14$), but were strongly correlated with report criterion ($r=0.67$; $p<0.0001$). Report criterion was inversely correlated with BSI somatisation ($r=-0.26$; $p=0.001$) and BSI global score ($r=-0.18$; $p=0.035$). Similar results were seen for the non-painful sensation of urgency.
Conclusion: Increased colonic sensitivity in IBS is strongly influenced by a psychological tendency to report pain and urge rather than increased neurosensory sensitivity.

During balloon distension of the rectum or colon patients with irritable bowel syndrome (IBS) report pain and discomfort at abnormally low volumes or pressures.[1–3] These lower pain thresholds have been interpreted to represent visceral hypersensitivity[4 5] and have been attributed to physiological differences in IBS patients.[6–8] Mertz *et al* even proposed that lower pain thresholds are "a reliable biological marker of IBS."[9] However, it is impossible to attribute lower IBS pain thresholds specifically to underlying physiological mechanisms[3 10] since cognitive and psychological influences affect the reporting of pain and, by extension, affect threshold measurements.[1 11 12]

The physiological and psychological components that determine pain thresholds can be separately quantified by sensory decision theory analysis (SDT).[13] In SDT stimuli of different intensities are presented in an unpredictable order and subjects rate the intensity of each stimulus. Statistical decision theory is then used to determine:

(1) The *discrimination index (p(A))*: a measure of neurosensory sensitivity (physiological) that is based on the subject's ability to discriminate between two stimuli of similar, yet distinct, intensities. The discrimination index is reduced by local nerve blocks and analgesics, but is immune to cognitive and psychological manipulations.[14 15]
(2) The *report criterion (B)*: a measure of the subject's overall tendency to label any stimuli as weak vs intense, independent of the actual stimulus intensity. The report criterion is susceptible to cognitive and psychological manipulations such as suggestion and placebo, but is not affected by analgesics.[14–16]

The primary aim of this study was to determine whether differences in pain thresholds between patients with IBS and healthy controls are explained primarily by differences in neurosensory sensitivity (physiological differences) or differences in the overall tendency to report pain (psychological differences). The secondary aim was to determine and explain differences in urge thresholds. Ultimately, a better understanding of the factors that affect these thresholds will improve our understanding of the mechanisms responsible for hypersensitivity and might help to direct therapy. Accordingly, we used AML to compare sensory thresholds in both IBS patients and healthy controls, and SDT supplemented by psychological questionnaires to determine how physiological and psychological factors contribute to these thresholds. We hypothesised that, compared to healthy controls, IBS patients would have: (1) lower AML determined pain and urge thresholds; (2) similar levels of neurosensory sensitivity; and (3) a lower report criterion (that is, an increased overall tendency to report stimuli as intense). (4) We also hypothesised that AML pain thresholds and the report criterion would be inversely correlated with levels of psychological distress.

Abbreviations: AML, ascending methods of limits; BSI, Brief Symptom Inventory; IBS, irritable bowel syndrome; IBS-C, constipation predominant irritable bowel syndrome; IBS-D, diarrhoea predominant irritable bowel syndrome; IOP, individual operating pressure; ROC, receiver operator characteristic; SDT, sensory decision theory analysis

METHODS

Subjects

Subjects were recruited by advertisements or physician referrals and screened by telephone. The study was approved by the institutional review board of the University of North Carolina (UNC) and all subjects provided informed consent.

IBS patients

The study population consisted of 132 patients (84% female; median age 35 years) who met Rome II criteria for IBS[17] and had current symptom activity (abdominal pain at least once a week in the past month). Twenty-seven IBS patients were constipation predominant (IBS-C), 31 were diarrhoea predominant IBS (IBS-D), and 61 were not classifiable as either. These subjects had no history of gastrointestinal resection (other than appendectomy or cholecystectomy), known IBS, coeliac disease, lactose malabsorption, heart disease, or diabetes mellitus, and they were not pregnant at the time of study. IBS patients were required to stop the following medications—antidepressants (seven days before study), antispasmodics, muscle relaxants or narcotic analgesics (three days); and non-steroidal anti-inflammatory agents (one day).

Controls

The control population consisted of 31 subjects (71% female; median age 40 years) without any significant or recurring gastrointestinal symptoms; exclusion criteria were average stool frequency of less than three per week or more than three per day, abdominal pain, use of a laxative or anti-diarrhoeal agent on more than two occasions over the previous year, history of alcohol or substance abuse, a psychiatric diagnosis, or any of the medical conditions listed above for the IBS patients. None of these healthy subjects had used any antidepressants, antispasmodics, muscle relaxants, or narcotic analgesics for at least one year. Non-steroidal anti-inflammatory agents were not permitted for at least one day before the study. There were no significant differences between the IBS group and healthy controls for age ($p = 0.72$) or sex ($p = 0.12$).

Psychological evaluation

On the first day of the study subjects reported to the UNC General Clinical Research Center (GCRC) at 11 am where they completed the Brief Symptom Inventory-18 (BSI-18). This is an 18-item measure of psychological distress along three primary symptom dimensions: somatisation, anxiety, and depression.[18] The BSI-18 was also scored for the global severity index. The rationale for including the BSI somatisation scale is that somatic hypervigilance is hypothesised to play a part in visceral hypersensitivity.[12] The BSI depression, anxiety, and global scales were included based on the convention of regarding depression and anxiety as the primary dimensions of psychological distress.

	Numeric rating	Descriptor	Beta value
	5	Intense	1
Boundary 5			
	4	Strong	2
Boundary 4			
	3	Moderate	3
Boundary 3			
	2	Mild	4
Boundary 2			
	1	Weak	5
Boundary 1			
	0	None	6

Figure 1 Subjects rated the intensity of each stimulus on the six point rating scale showed above. The corresponding descriptor and beta value for each numeric rating are shown. Boundaries separate consecutive ratings.

Colonic sensory testing

At approximately 4 pm subjects underwent bowel preparation with 3 oz of Fleets Phospho-Soda followed by an overnight fast. On the morning of the second day (approximately 8 am) a barostat catheter was placed into the descending colon for sensory testing. Firstly, a guide wire was inserted to the level of the splenic flexure using a flexible sigmoidoscope. The sigmoidoscope was then withdrawn and a barostat catheter (Model No C7-CB-0026, Mui Scientific, Mississauga, Ontario, Canada) was inserted over the guide wire. The guide wire was then withdrawn and barostat placement was confirmed by fluoroscopy. No sedation was used throughout the duration of this procedure. A 600 ml plastic bag (Model No CT-BP600R, Mui Scientific, Mississauga, Ontario, Canada) was attached to the catheter, and the catheter was connected to a computer controlled piston type pump (barostat) that was capable of inflating and deflating the bag at a rate of 38 ml/s (G&J Electronics, Willodale, Ontario, Canada). The pump was interfaced to a computer running a software program that recorded the pressure inside the bag 16 times per second.

Subjects were instructed to give separate ratings of the intensity of pain and urgency to defecate experienced at the end of each distension, using a six point scale (0 = no sensation; 1 = weak; 2 = mild; 3 = moderate; 4 = strong; 5 = intense) (fig 1). The scale was visible to subjects during the procedure. Sample distensions were then performed during which the barostat bag was inflated in a stepwise fashion by increasing bag pressure by 4 mm Hg every 15 seconds until the subject reported moderate pain (rating of 3). The purpose of the sample distensions was threefold: (1) to insure that the barostat bag was unfolded; (2) to teach the subject how to use the rating scale to rate the intensity of colonic sensations; and (3) to decrease anticipatory anxiety. The barostat bag was then slowly inflated with 30 ml of air and the pressure was allowed to equilibrate for 3 minutes. The average pressure during the last 15 seconds defined the individual operating pressure (IOP): the minimum pressure required to overcome mechanical forces and inflate the bag with 30 ml of air.

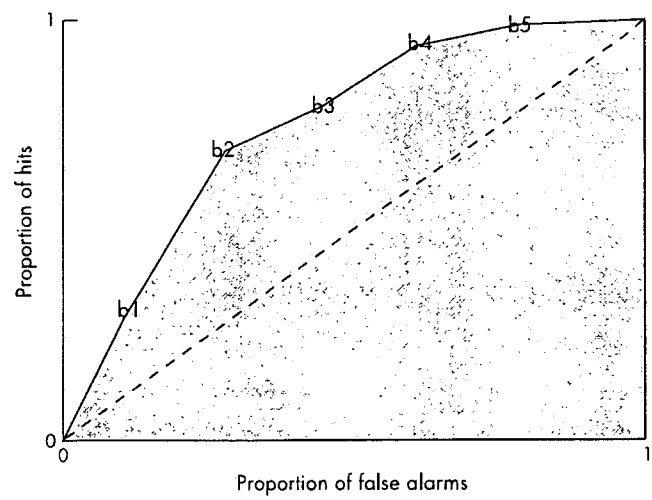

Figure 2 Receiver operator characteristic curve (ROC curve): each point represents the proportion of hits and false alarms for a given boundary (b1–b5). The total area under the ROC curve represents p(A).

Ascending method of limits (AML) protocol

This protocol started approximately 90 minutes following barostat placement. Phasic distensions were 30 seconds in duration and were separated by 30-second rest intervals starting at the IOP and progressively increasing in 2 mm Hg steps until either the subject requested the research nurse to stop the protocol or 48 mm Hg was reached. The pain threshold was defined as the amount of pressure above IOP at which the subject first reported moderate pain (absolute distending pressure minus the IOP). If the subject requested that the research nurse stop the trial before moderate pain was reported (for example, because of urge to defecate) then the pain threshold was not determined. If the subject reached 48 mm Hg without reporting moderate pain, then the pain threshold was defined as 50 mm Hg minus the IOP. The urge threshold was defined analogously.

Sensory decision theory (SDT) protocol

This protocol started approximately 100 minutes following barostat placement. Subjects were instructed that the purpose was to evaluate how well they could discriminate between different balloon pressures. Twenty-four 30-second phasic distensions (eight at 30 mm Hg, eight at 32 mm Hg, and eight at 34 mm Hg) were presented in an unpredictable order separated by 30-second rest intervals at the IOP. These stimulus intensities were selected to bracket the average pain threshold determined by AML in a previous study of SDT.[19] The choice of 2 mm Hg increments between stimuli was based on this previous study in which this difference was found to work well (that is, subjects made some errors of classification but discrimination was better than chance).[19] This protocol followed the recommendation of McNicol[20] and one of the co-investigators who is an expert on SDT (WCC). The subjects were able to stop the protocol at any time.

Discrimination index (p(A)) and report criterion (B) values for the 30 mm Hg vs 34 mm Hg stimuli were calculated for each subject using a computer program developed by MN Janal and WC Clark (personal communication). This program was based on formulas taken from McNicol for non-parameteric SDT analysis of rating scale data.[20]

The meaning of the discrimination index (p(A)) is clear: it is a measure of the ability to distinguish between the two stimulus intensities, based on the sensory intensity ratings reported in response to them. However, the computational formula is complex: (1) ratings on the rating scale used by the subject to subjectively rate the intensity of stimuli that are presented, are separated by multiple boundaries (fig 1). (2) For each boundary one calculates the proportion of all the higher intensity stimuli (that is, 34 mm Hg distensions) that received ratings above this boundary (this is the "hit" rate for this boundary) and one separately calculates the proportion of the lower intensity stimuli (that is, 30 mm Hg distensions) that received ratings above this boundary (this is the "false alarm" rate for this boundary). Thus, in this study hit rates and false alarm rates were calculated for each of five boundaries. (3) These hit rates and false alarm rates are plotted against each other to create a receiver operator characteristic curve (ROC curve) as shown in figure 2. The curve is drawn by connecting the different intersections of hit and false alarm rates calculated for each boundary (shown by the solid line in fig 2). (4) P(A) is the total area under the ROC curve (shaded area in fig 2) expressed as a proportion of the maximum possible area. The broken diagonal line in figure 2 goes through all the points for which the hit rate and the false alarm rates are equal; this represents chance performance or no discrimination, and the index, p(A) is 0.5. All values less than 0.5 are considered chance performance and are rounded up to 0.5. Thus, p(A) is a number between 0.5 (chance) and 1.0 (perfect discrimination) that measures the ability to discriminate between the two intensities independently of what rating labels the subject uses to describe the stimuli.

The report criterion (B) is the median rating assigned by the subjects to all stimuli. Firstly, the ratings assigned to the

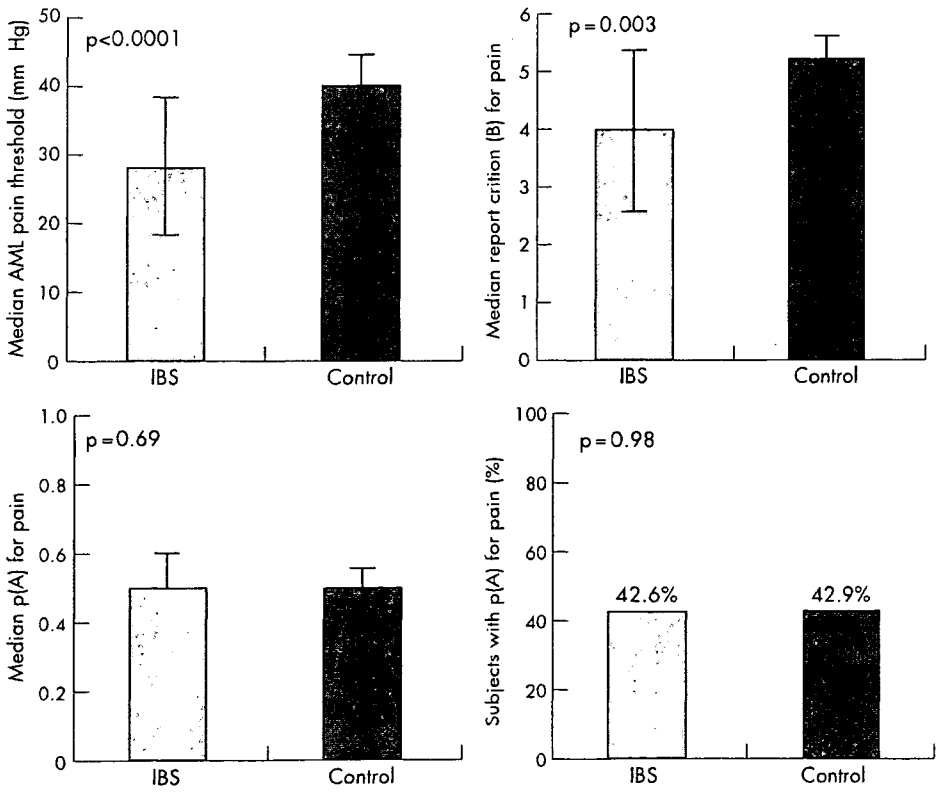

Figure 3 (Top left) Median AML pain thresholds: thresholds were significantly higher in healthy controls than in IBS subjects. (Top right) The pain report criterion (B) across both 30 mm Hg and 34 mm Hg stimuli: IBS patients had a lower criterion, which reflects their increased tendency to report pain irrespective of stimulus intensity. (Bottom left) The median pain neurosensory sensitivity (p(A)). There were no differences between the two groups. (Bottom right) The percentage of subjects whose ability to discriminate painful sensations between 30 mm Hg and 34 mm Hg stimuli was better than chance (p(A)>0.5): there was no difference between the two groups. The bars on each graph represent the interquartile range.

30 mm Hg distensions were pooled with ratings for the 34 mm Hg distensions. Secondly, each response on the six-point rating scale was assigned an individual report criterion (B) value. Based on SDT convention, a numerically low criterion means a "liberal" tendency to rate most of the stimuli as intense, whereas a numerically high criterion means a "conservative" or "stoic" tendency to label most stimuli as less intense. Therefore, higher (that is, more intense) subject ratings are assigned lower B values and vice versa (fig 2). Thirdly, the overall report criterion (B) was determined as the B value on the six point rating scale for which half of total responses to *both* stimulus intensities were to categories above the criterion and half were to categories below the criterion.[13]

There was a strong correlation between AML pain thresholds and pain report criterion ($r = 0.67$ $p<0.0001$). On the contrary, AML pain thresholds did not correlate with neurosensory sensitivity for pain ($r = -0.13$; $p = 0.14$).

Data analysis

The data were not normally distributed. Consequently, non-parameteric statistical tests were used. Significance was set at a p value of 0.05. Firstly, Wilcoxon rank sum tests were used to compare IBS patients to controls with respect to the following measures: AML determined pain and urge thresholds; SDT determined pain and urge discrimination index (p(A)) and report criterion values (B); BSI anxiety, depression, somatisation, and global severity index scores. Secondly, Spearman correlations were used to determine associations between AML pain thresholds with SDT determined pain discrimination index (p(A)) and report criterion (B). Thirdly, Spearman correlations were used to determine associations between both AML pain thresholds and pain report criteria (B) with the following measures: p(A), BSI anxiety, depression, somatisation, and global severity index scores.

RESULTS

Excluded subjects

In all, 119 IBS patients and 29 control subjects underwent colonic sensory testing. Of the 13 IBS patients who did not undergo colonic sensory testing, three withdrew consent after the first day, possibly because of apprehension regarding the pain test procedure, three refused flexible sigmoidoscopy, two did not tolerate sigmoidoscopy, one had an extremely elevated blood pressure, and one had colonic inflammation detected on sigmoidoscopy. Of the three excluded control subjects, one did not tolerate the flexible sigmoidoscopy and two had exclusionary medical conditions that were detected during the study (lactose intolerance in one and previous colonic surgery in the other).

Pain thresholds, neurosensory sensitivity, and report criterion

On the AML protocol IBS patients had lower pain thresholds (median 28 mm Hg vs 40 mm Hg; $p = 0.0002$). On sensory decision theory analysis there were no differences in pain neurosensory sensitivity (median p(A): 0.5 vs 0.5; $p = 0.69$; 42.6% of IBS patients vs 42.9% of healthy controls had p(A) >0.5 (chance); $p = 0.98$). Conversely, IBS patients had a lower pain report criterion, which represents their increased tendency to report stimuli as being relatively painful irrespective of the actual intensity of the stimulus (median B: 4.0 (median response = mild pain) vs 5.2 (median response = weak pain); $p = 0.003$) (fig 3).

Table 1 Psychological profiles of IBS and control populations

	IBS median (range)	Controls median (range)	p Value
BSI global severity index	49 (33–78)	42 (33–63)	<0.0001
BSI anxiety	50 (38–74)	39 (38–61)	<0.0001
BSI depression	48 (40–81)	42 (40–61)	=0.006
BSI somatisation	55 (41–74)	41 (41–66)	<0.0001

Psychometric scores and pain report criterion

IBS patients scored higher than controls on all psychometric scales (table 1). There were modest inverse correlations between pain report criterion (B) and BSI global score ($r = -0.18$; $p = 0.035$) and BSI somatisation ($r = -0.26$; $p = 0.001$) (table 2). Higher psychological distress correlated with an increased tendency to report pain.

Urge thresholds, neurosensory sensitivity, and report criterion

Sensory thresholds for urge were lower than those for pain. On the AML protocol IBS patients had lower urge thresholds than controls (median: 18 mm Hg vs 34 mm Hg; $p = 0.002$), but on sensory decision theory analysis there were no differences in urge neurosensory sensitivity (median p(A): 0.55 vs 0.50; $p = 0.17$; 63.1% of IBS patients vs 46.4% of healthy controls had urge p(A) >0.5 (chance); $p = 0.10$). Conversely, IBS patients had a lower urge report criterion, which represents their increased tendency to report relatively intense urge irrespective of the actual intensity of the stimulus (median B: 3.0 (median response = "moderate" urge) vs 4.2 (median response = "mild"); $p = 0.006$) (fig 4).

There was a strong inverse correlation between AML urge thresholds and urge report criterion ($r = -0.51$; $p<0.0001$) and a weaker but significant inverse correlation with neurosensory sensitivity to urge ($r = -0.22$; $p = 0.007$).

Psychometric scores and urge report criterion

There were modest inverse correlations between urge report criterion (B) and BSI global score ($r = -0.19$; $p = 0.03$), BSI somatisation ($r = -0.18$; $p = 0.04$), and BSI anxiety ($r = -0.17$; $p = 0.05$) (table 3). Higher psychological distress correlated with an increased tendency to report urge.

Additional analyses of SDT data

There was a moderately strong positive correlation between pain and urge discrimination (p(A)) ($r = 0.50$; $p<0.0001$). Similarly, there was a moderately strong positive correlation between pain and urge report criteria (B) $r = 0.44$; $p<0.0001$).

The SDT test involved 24 distensions at pressures, which were painful for most subjects, and consequently some subjects did not complete all trials. The accuracy of discrimination index (p(A)) and report criterion (B) values in subjects who underwent fewer SDT distension trials might have been lower because of increased variance. We therefore excluded subjects who completed fewer than one-half (<12) of all trials (33 IBS, 4 controls, $p = 0.158$) and repeated the comparison between IBS patients and controls for pain p(A) and report criterion (B). The pattern of results and the significance of the differences did not change for pain p(A) (median p(A) 0.5 vs 0.5; $p = 0.31$; % with pain p(A) > chance: IBS = 47.1%; control = 41.7%; $p = 0.63$;) or pain report criterion (median B: IBS = 4.4; control = 5.4; $p = 0.0001$).

Repeated distension of the colon has been previously shown to induce hyperalgesia ("sensitisation") in IBS patients.[5] Thus, it is possible that as a result of this potential sensitisation, the intensity ratings made by IBS patients to late SDT trials may

Table 2 Spearman's correlations: AML pain threshold and pain report criterion (B)

	Correlation (rho) with AML pain threshold	Correlation (rho) with SDT pain report criterion (B)
Pain p(A)	−0.13 p=0.1	−0.16 p=0.04
Pain B	0.67 p<0.0001	–
BSI global severity index	−0.22 p=0.01	−0.18 p=0.04
BSI anxiety	−0.11 p=0.2	−0.04 p=0.7
BSI depression	−0.11 p=0.2	−0.07 p=0.4
BSI somatisation	−0.28 p=0.001	−0.26 p=0.001

Table 3 Spearman's correlations: AML urge threshold and urge report criterion (B)

	Correlation (rho) with AML urge threshold	Correlation (rho) with SDT urge report criterion (B)
Urge p(A)	−0.22 p=.007	−0.09 p=0.3
Urge B	−0.51 p<0.0001	–
BSI global severity index	−0.19 p=0.03	−0.18 p=0.04
BSI anxiety	−0.17 p=0.05	−0.15 p=0.07
BSI depression	−0.07 p=0.4	−0.12 p=0.15
BSI somatisation	−0.18 p=0.04	−0.16 p=0.06

have been affected. In order to test for this we first determined the change in pain intensity ratings between the first and the last 30 mm Hg and 34 mm Hg trials (change in ratings = pain intensity rating to the last 30 mm Hg stimuli plus pain intensity rating to the last 34 mm Hg stimuli minus pain intensity ratings to the first 30 mm Hg stimuli minus pain intensity rating to the first 34 mm Hg stimuli). We then used the Wilcoxon rank sum test of differences to compare change in intensity ratings between IBS patients and controls who completed at least one-half (≥12) of all trials. There was no difference between the two groups (p = 0.22).

Finally, the intensities of the three SDT stimuli (30 mm Hg, 32 mm Hg, 34 mm Hg) were below AML pain thresholds for some subjects (mostly controls) and above threshold for other subjects (mostly IBS patients). Therefore, it was possible that certain subjects failed to demonstrate discrimination (p(A)) because they assigned the same ratings to all stimuli (either calling all of them "intense" or calling all of them non-painful). We identified nine (7.4%) IBS patients and nine (35%) healthy controls who rated each SDT stimulus as zero pain intensity. One IBS patient rated all stimuli as "intense." All other subjects varied their pain intensity ratings. When we excluded the 10 IBS patients and nine healthy controls who did not vary their pain intensity ratings and repeated the analysis, the pattern of results and the significance of the differences did not change for pain p(A) (median p(A) 0.5 vs 0.52; p = 0.8); percentage with pain p(A) > chance: IBS = 45.6%; control = 52.2%; p = 0.57) or pain report criterion (median B: IBS = 3.9; control = 4.52; p = 0.04).

DISCUSSION

In this study we first used AML to measure pain and urge thresholds and we then used SDT to determine the two components of these thresholds: physiologically determined neurosensory sensitivity and psychologically determined report criterion. Using these techniques, we demonstrated that lower AML determined pain and urge thresholds in patients with IBS are explained primarily by an increased tendency to report pain and urge, not increased neurosensory sensitivity. Since this lower report criterion reflects psychological phenomena, increased colonic sensitivity in IBS appears to be determined more by psychological factors than by physiological factors.

Pain is a complex perceptual experience that can only be measured indirectly.[21] Gastrointestinal pain sensitivity is typically measured by pain thresholds, which are defined as the lowest stimulus intensity to which subjects report pain. However, pain

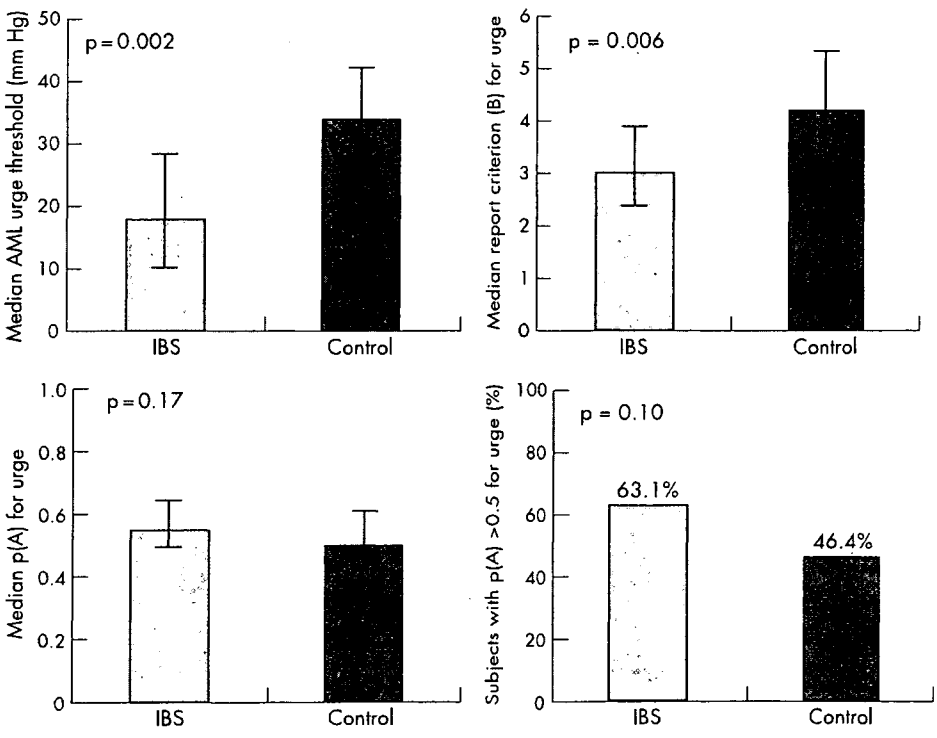

Figure 4 (Top left) Median AML urge thresholds: thresholds were significantly higher in healthy controls than IBS subjects. (Top right) The median urge report criterion (B) to 30 mm Hg and 34 mm Hg stimuli: IBS patients had a lower criterion which reflects their increased tendency to report urge irrespective of stimulus intensity. (Bottom left) The median urge neurosensory sensitivity (p(A)). There were no differences between the two groups. (Bottom right) The percentage of subjects whose ability to discriminate urge sensations between 30 mm Hg and 34 mm Hg stimuli was better than chance (p(A)>0.5): there was no difference between the two groups. The bars on each graph represent the interquartile range.

thresholds are not equivalent with painful sensations since pain reports are influenced by non-neurosensory factors such as placebo, emotion, attention, and distraction.[13]

SDT is an alternative pain measurement technique that separately quantifies the individual components of the pain response: neurosensory sensitivity (p(A)), a measure of neurosensory function based on the ability to discriminate between stimuli; and report criterion (B), a measure of stoicism based on the overall tendency to report pain.[13] Importantly, previous research has shown that only the criterion is susceptible to changes in cognitive or psychological variables.[13–15] The discrimination index, p(A), changes in response to analgesic drugs but is not influenced by psychological manipulations.[15 16] In this study, IBS patients had similar pain neurosensory sensitivity and lower pain report criterion compared to healthy controls. In other words, their tendency to report pain at lower thresholds related not to increased neural sensitivity, but rather to their predilection towards reporting pain.

Whereas SDT has been widely used in somatic pain research[13] it has been used only rarely in previously published studies on visceral pain sensitivity in functional gastrointestinal disorders. Bradley *et al* observed lower AML pain thresholds, similar neurosensory sensitivity, and decreased report criterion for balloon distensions of the oesophagus in patients with non-cardiac chest pain,[22] which is similar to the findings of this study. Whitehead *et al* observed lower AML pain thresholds and similar neurosensory sensitivity for rectal distensions in women with IBS,[19] which is also similar to the findings of this study. However, they did not measure the report criterion.

Similar to pain, our findings also suggest that lower AML determined urge thresholds in patients with IBS are largely explained by an increased tendency to report urge. However, the finding that urge thresholds and urge neurosensory sensitivity were inversely correlated ($r = -0.22$, $p<0.005$) suggests that lower urge thresholds in IBS may also be attributable—albeit to a lesser extent—to increased urge neurosensory sensitivity. These findings contrast with those reported by Corsetti *et al* who, using non-painful, barely perceivable balloon distensions, found that patients with IBS had increased neurosensory sensitivity and similar report criterion. However, unlike our study, their study involved a small population (22 patients and 13 controls) in which there were no psychological differences between the IBS and control groups.[23]

The increased tendency to report pain and urge in patients with IBS may be the downstream result of multiple cognitive and psychological processes. Firstly, patients with IBS appear to be hypervigilant to gastrointestinal sensations.[12 24] For example, on functional brain imaging they show similar, abnormal cortical responses to both actual and anticipated (sham) distensions.[25 26] Secondly, hypervigilance may reduce the intensity at which they notice gut distensions[28] and sensations. Thirdly, once perceived, subjects with IBS interpret these sensations through a generally negative schema (framework for explaining reality),[28] which leads them to attribute their sensations to disease.[29] Finally, disease attribution in turn further increases attention to gastrointestinal symptoms[30] through which a cycle of gastrointestinal sensory amplification is ultimately established.[31] Along these lines, in our study somatisation was more common in IBS and was correlated inversely with pain thresholds and directly with the response criterion. This is similar to findings that in Gulf War veterans with IBS, lower pain thresholds could be largely explained by increased somatic focus.[32] Other investigators have also found that global psychological distress is correlated with the amount of brain activation in response to painful rectal distension[33] and is inversely correlated with tolerance for painful balloon distension of the rectum.[34]

In order to assess visceral sensitivity independently from these cognitive processes, some have proposed measuring cortical activity during subliminal distensions (that is, not consciously perceived).[35 36] Lawal *et al* used this approach and found increased cortical activation in subjects with IBS. They interpreted this as evidence for neural hypersensitivity that is independent of cognitive input.[37] However, it is unclear whether these distensions were truly subliminal since most individuals can perceive distensions as small as 5 mm Hg[38]; the distensions in their study ranged from 10 mm Hg to 20 mm Hg. Secondly, their observation that cerebral activation in IBS patients did not increase in a positive dose-response fashion suggests that IBS patients were globally hypersensitive at baseline. This global hypersensitivity was attributed by Naliboff and Mayer to cognitive and psychological processes such as uncertain expectation and hypervigilance, that could not be completely controlled for in the study.[39]

Although our data demonstrate that psychological phenomena strongly influence pain thresholds, our experimental methods may not have been sensitive enough to detect subtle differences in neurosensory sensitivity. Thus, we cannot rule out the effects of peripheral physiological mechanisms, such as sensitisation of colonic afferent pathways.[6 42 43] This afferent hypersensitivity has been credited to inflammation based on evidence that experimentally induced colonic inflammation lowers rectal pain thresholds in animal models.[42] Nonetheless, inflammation has not been shown to explain lower thresholds in IBD patients.[43 44]

Study limitations

Two potential limitations to this study were posed by the repeated balloon distensions required by the SDT protocol. Firstly, certain subjects failed to complete all 24 SDT trials because of intolerable levels of pain or urge. We estimated the effects of this by repeating our analyses without including those subjects who completed fewer than half of the trials. The results were the same. Secondly, the process of repeated very intense colonic distensions (60 mm Hg) has been previously shown to induce rectal hypersensitivity in subjects with IBS.[8] We estimated the effects of this by comparing the change in pain intensity ratings between early and late stimuli in IBS patients and healthy controls. There was no difference between the two groups.

SDT, which quantifies the ability of subjects to discriminate between very similar stimuli, required that we use stimulus intensities that were very close to each other (30 mm Hg vs 34 mm Hg). This might have been too close to allow for adequate discrimination—that is, the measurement of neural sensitivity may have been insensitive. However, most subjects can perceive a 5 mm Hg increase in stimulus intensity.[19] In this study 43% of both IBS patients and healthy controls were able to discriminate between the 30 mm Hg and 34 mm Hg distensions at better than chance levels (p(A) values above 0.5).

Calculation of the report criterion required us to use the same stimuli for all subjects, irrespective of their AML thresholds. As a result, the ability of some subjects to discriminate between SDT stimuli might have been affected either because the test stimuli were well above their pain threshold or they were so far below their pain threshold that none of them were perceived as painful. We tested for this by excluding subjects who rated all stimuli as equally painful and repeating the analysis. The results did not change. Furthermore, in our previous smaller study where we individualised SDT stimulus intensities for each patient based on their AML determined pain threshold (though we did not compute a report criterion), we still found

that subjects with IBS and healthy controls had similar neurosensory sensitivity to pain.[19]

A theoretical limitation is that we used pressure rather than volume based balloon distensions. Some investigators prefer volume based distensions or indices that integrate pressure and volume into estimates of wall tension.[45] We followed the recommendations of an international consensus committee[46] by scaling our distensions in pressure rather than volume because it is recognised that volume thresholds are influenced by muscle tone, which varies from hour to hour in response to meal ingestion and anxiety. Individual differences in pain thresholds are believed to be more stable and reproducible when measured on a pressure scale rather than a volume scale.

Conclusion

These data show that lower pain and urge thresholds in subjects with IBS are strongly influenced by cognitive and psychological factors. Peripheral physiological events such as inflammation[42] and temporal summation[6] have also been shown to influence pain sensitivity. However, these data suggest that, when explaining the differences between IBS patients and healthy controls, the contribution of peripheral physiological events may be relatively small compared to the cognitive and psychological influences that are reflected in the report criterion index, which reflects the generalised tendency to report pain. The implications of this finding are far reaching. Firstly, it underscores the importance of accounting for psychological factors when interpreting tests of sensory function. Secondly, it highlights the important part played by centrally mediated processes in the pathophysiology of visceral sensitivity in IBS and suggests that novel therapies for pain in IBS should target centrally mediated mechanisms.

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EDITOR'S QUIZ: GI SNAPSHOT

Answer

From question on page 1190

The echocardiogram demonstrates a pericardial effusion with cardiac tamponade. This resulted in ischaemic hepatitis (IH) and acute liver failure (ALF). An emergency pericardiocentesis was performed, and circulatory function immediately improved. Liver and renal function normalised over the next 15 days (fig 1).

IH is an uncommon but well described cause of ALF. In this case, ischaemic liver injury occurred because of a combination of factors: right heart failure (acute hepatic congestion) and decreased hepatic arterial perfusion, secondary to hypotension from cardiac tamponade.

IH occurs in the setting of the following predisposing factors: reduced hepatic arterial flow states, passive liver congestion and arterial hypoxaemia. Aetiologies include cardiac arrest and intraoperative hypotension (eg, cardiac bypass) on a background of respiratory or left ventricular failure.

Treatment aims at removing the insult to the liver and maximising cardiac output, thus improving oxygenation. Fulminant hepatic failure is uncommon, and usually occurs with pre-existing cirrhosis. The condition is reversible, depending on the underlying cause of the circulatory insult. Because of the setting of major circulatory failure (eg, cardiac arrest) and good prognosis if circulation is restored, liver transplantation is rarely indicated.

When presented with ALF, it is important to consider ischaemia, a reversible condition. Although cardiac tamponade is a rare cause of IH, this case demonstrates the benefit of early diagnosis and removing the insult to the liver with resultant rapid and complete clinical improvement of the IH.

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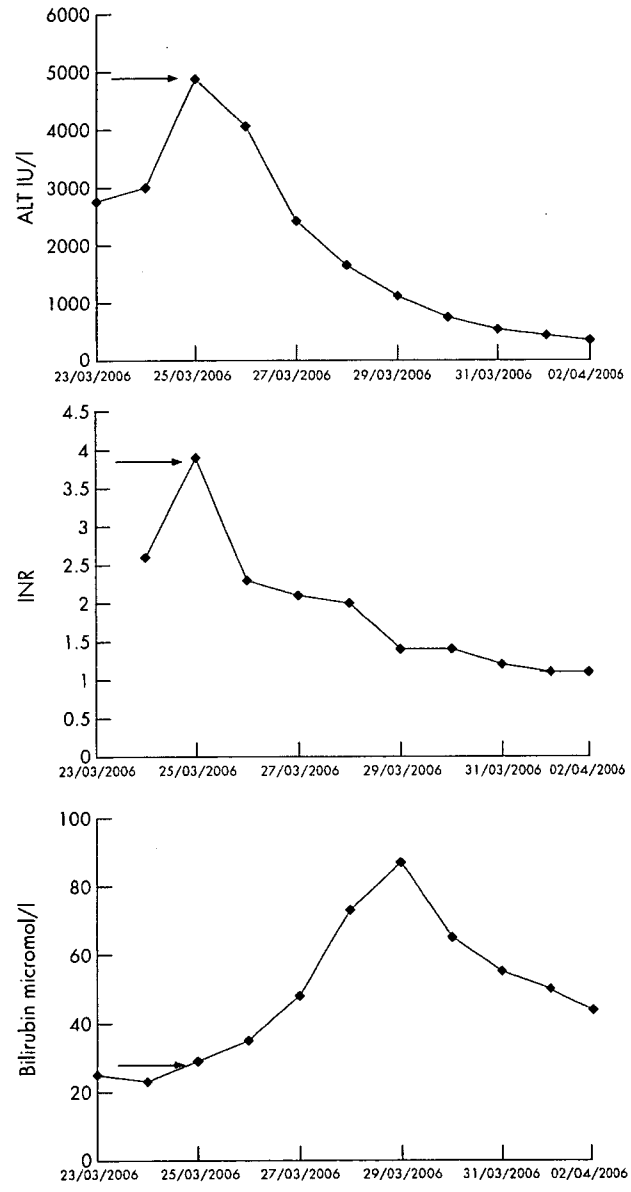


Figure 1 Graphs showing the biochemical changes in the reported case. The acute rise and fall in alanine aminotransferase (ALT) and international normalised ratio (INR), with a delayed rise in bilirubin, are characteristic of ischaemic hepatitis. The arrows denote when pericardiocentesis was performed.

IV. 新聞・報道等

NAVIGATOR

過敏性腸症候群

頻繁な下痢や便秘、腹痛で通勤にも困るほど。どうしたら改善する。

代表的なストレス病

主に10～20代　5月に多い発症

「ひどい時は、通勤途中に電車が駅に停車するたびに降りて、トイレに駆け込んだ」。東京都内の30代の男性会社員は、中学生のころから試験の時などにおなかを下しがちだったが、就職後は通勤にも困るほど頻繁に下痢をするようになった。

満員電車の中で動けないというストレスが症状を悪化させたため、職場の近くに引っ越したこともあった。神経内科に通院しても、抜本的な改善にはつながらず、人前で話すような仕事の2～3日前からビールを飲まなかったり、食事の量を減らすなど独自の工夫で乗り切っている。

男性のような症状の病気は「過敏性腸症候群」と呼ばれる。内視鏡などで調べても腸に潰瘍などの異常はないのに、腸がうまく働かない病気だ。

腹痛やおなかの不快感に下痢や便秘を伴う。慢性的に出るおならに悩む人も少なくない。

医師でも悩まされている。関東の大学病院に勤務する30代の消化器内科医の男性は、自身が過敏性腸症候群の患者だ。中学3年ごろから下痢をしやすくなり、今でも単に長時間乗る前などは、朝食を抜いて下痢止めを飲み、成人用おむつも用意する。自分が診察していた患者の中には、薬を服用しても下痢などの症状をコントロールできず、通勤できなくなって会社を辞めざるを得なかった人や、まったく外出できない人もいるという。

男性は「生命を左右する病気でないために、医師や行政、製薬会社も関心が薄いのではないか。患者が通院しなくなったり、転々と病院を変えるケースも多く、患者の実態がつかめないことも研究が進んでいない一因だ」と話す。

＊

福土審・東北大教授（行動医学）は「過敏性腸症候群は代表的なストレス病」と話す。患者は10～20代に多く、国内の患者数は人口の14％程度に達するとみられる。入学、入社後の5月に発症する人も多い。ストレスによって症状は悪化し、年齢を重ねたり、ストレスの原因を避けることで改善するという。

福土教授によると、最近の研究から、発症には「脳腸相関」と呼ばれるメカニズムも関係しているとみられる。ストレスを感じると、脳から腸に信号が送られ、腸の運動に異常を生じさせるらしい。しかし、不明の点も多いのが実情だ。

診断は、国際的な診断基準などを基に行う。治療は薬の服用と生活指導が中心だ。三木内科クリニック（東京都千代田区）の三木治院長（内科、心療内科）によると、患者の症状に合わせて下痢止めや鎮腸剤などの他、不安感が強ければ抗不安薬などを処方する。

食生活や嗜好品を見直すことも重要だ。三木院長は「消化器を過剰に刺激しない食事、飲み物が基本」と話し、ソ辛いコーヒーソ炭酸飲料ソスパイスの利いた辛い料理ソ脂っこい料理――などは避けるよう勧める。下痢が続いて適正に食事が取れない時に栄養ドリンクを飲む患者もいるが、ドリンクに含まれるカフェインや炭酸が腸を刺激するので注意した方がいい。

＊

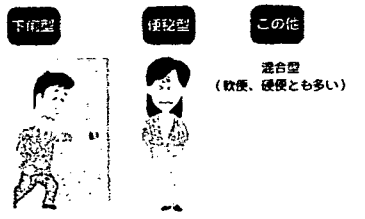
周囲の気遣いも欠かせない。特に、子どもの場合は下痢や便秘などで頻繁にトイレに行くような場合に家族が声をかけ、場合によって治療を受けさせることも必要だ。

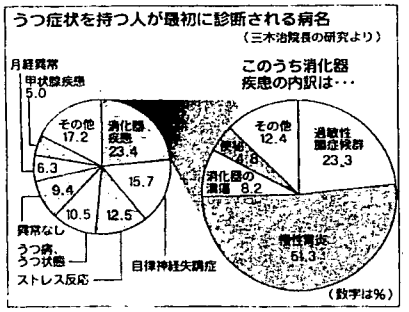
大人でも単に「ストレス病」ですまない場合もある。三木院長の調査によると、うつ症状のある患者の4人に1人は、最初にかかった医療機関で消化器疾患と診断され、うち23・3％は過敏性腸症候群だった。三木院長は「中高年になって腸の状態がよくなった後に、うつ病だったと分かる患者もいる。医師や周囲の人が、患者が訴える主な症状以外にも、他の病気や原因に気づいてあげることが大切だ」と話す。

過敏性腸症候群の診断基準（国際基準）

○腹痛か腹部不快感が一定日数（※）ある
※一定日数とは、過去3カ月の中のどこかの1カ月間で少なくとも3日以上のこと（連続しなくてもよい）
○下記の2項目以上が当てはまる
①排便によって症状が改善する
②排便の頻度が変わる
③便の外見が変わる（例：下痢がちになるなど）

過敏性腸症候群の分類





原因避け 食生活見直し 整腸剤、抗不安薬で治療 うつ病の可能性も

「第2の脳」不明点なお

腸は「第2の脳」と呼ばれるほど複雑な臓器だ。渡辺守・東京医科歯科大教授（消化器内科）によると、最近10年の研究で、脳部を除く体全体にある微小血管の55％やリンパ球の60％、多くのホルモンが腸に集まっていることなどが判明。過敏性腸症候群が起きる原因を考える手がかりがだいぶ解明されてきた。

過敏性腸症候群は「見た目に異常がない」ときに炎症などの異常がみつかったという報告も増えている。感染性大腸炎を発症した後には、過敏性大腸炎になりやすいという仮説もある。

渡辺教授は「過敏性腸症候群は糖尿病やうつ病と同じくらい生活の質を低下させるが、患者の75％以上は医療機関を受診していない。今後の研究で、発症の仕組みが明らかになれば薬物療法も確立されていくのではないか」と期待する。

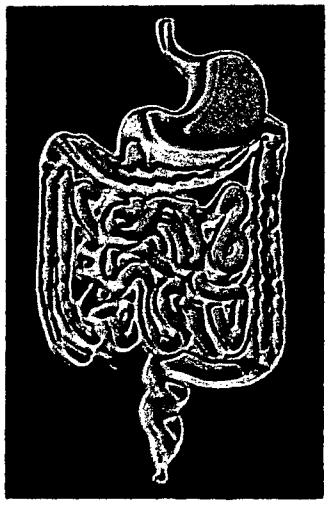
【大場あい】

内臓感覚

脳と腸の不思議な関係

福土 審

Fukudo Shin



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日本放送出版協会

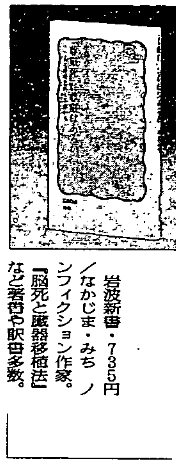
読書

■「尊厳死」に尊厳はあるか

最後の一瞬ま

一般外科医における延命措置の中止等に関する法律案要綱（案）」が公表された。
これに対し、本書の著者は患者の視点に立ち、当該医師や院長、患者の家族など関係者へのインタビューを通じて、事件の徹底した事実確認の作業を進める。
移植臓器の提供者が少ない日本では、臓器移植を促進するための環境整備を急ぐ動きもある。だが、著者の「足によるルポ」を通じて現れてきたのは、医師が可能な限りの

…はならないと指摘する。例えば、医師から「回復の見込みがない」と断言されれば、それに反論するだけの知識を持ち合わせない患者の家族にとっては、医師の言葉を受け入れざるを得なくなる。
臓器移植に尽力する人たちの努力を多とするが、こうした医療現場における改善を行った上で最後の一瞬まで尊厳ある生が守られてこそ「尊厳死」が成立する。医師に対する患者の信頼があってはじめて臓器移植への理解者もふえるのではないだろうか。



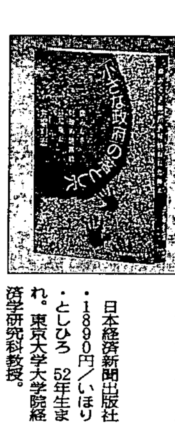
岩波新書・735円
／なかじま・みち ノンフィクション作家。『脳死と臓器移植法』など著書多数。

■「小さな政府」の落とし穴

最適規模を探

自助努力と自己責任を基本にして生きることが求められる。実際、著者によれば公的年金は「老後の生活に必要な最小限の給付（基礎年金）に限定し」、支給開始も男性75歳、女性80歳と年齢を引き上げ、医療保険も一律に給付するのではなく若いときから健康管理を「きちんと行ってきた人を優遇する仕組み」が望ましいという。
こうした提案の背景には、北欧に比し人口の大きな日本では受益と負担に関する国民

て軽くない。それでもセーフティーネットが厚くなるなら容認できる面もあるが、現在よりも薄くなるなら何のための負担増かと問いたくなる。
小さな政府に固執した小泉元首相の戦略を著者は、「意図的に財政赤字を拡大させ……小泉後の政権ではこれ以上財政赤字を拡大できない」ようにした点で、「したたかな財政運営」だったと評価するが、最終的なツケを回される国民にとってはむしろ「とんでもない財政運営」だったのではないだろうか。



日本経済新聞出版社・1890円／いほり・としひろ 52年生まれ。東京大学大学院経済学研究科教授。

半。問い合わせは中野書店（03・3261・3522）。
「行こう」（http://go-jimbou.info/）は、町の公式書店情報サイト「BOOKTOWNじんぼう」と公式タウンサイト「ナビブラ神保町」への扉にもなっているサイト。地元の人が街を紹介する「私の神保町」や、おすすめ散歩コースを案内する「神保町散歩道」などもある。

日本の無形文化国際的視点で

世界遺産の「無形文化財」版、ユネスコ「無形文化遺産」リストへの初登録が09年9月と決まり、伝統芸能や民俗文化の国際的な保護に関心が高まるなか、『世界遺産時代の村の踊り』が刊行された。著者の星野紘氏は文化庁で長年、民俗芸能保護行政に携わった研究者。日本各地の無形文化財を、ユーラシア大陸の伝承とも比較、関連づけながら論じている。雄山閣、3990円。

■知られざる魯山人 山田 和〔著〕

美の追求者の迫力を十分に

書、篆刻、陶芸、さらに星岡茶寮を中心に展開された料理など、美の追求者としての魯山人の評価は、ますます高まる一方だ。他方で、身勝手で傲岸不遜。傍若無人の言動。「唯我独尊」だったと噂される。こういった二つの顔が、関心を余計集めているのだろう。
父親に親交があったという著者が、膨大な参考文献を徹底的に渉猟、さらに多くの関係者にも取材し、「魯山人とは何か」に迫ったのが本書。おもしろい。
まず、謎めいた「賤しい不分明な出自」。生まれへの絶望的感情が芸術活動の源であったという。奉公先で、のちの竹内栖鳳の行灯看板絵に心動かされ、そこから美への彷徨が始まる。扁額（大板に文字を彫る看板）で名を上げる。各地で見聞を広げ、また多くの数寄者、茶人と交流し、次第に創造の世界が広がる。
青山二郎、荒川豊蔵、加藤唐九郎、山口淑子、イサム・ノグチ、小林秀雄、棟方志功、政財界の面々。登場する交友名も豪華だ。果たし合いに近い歯にきぬ着せぬ批評の応酬。
周りにいたものはさぞかし大変だったろうな、と思わせるエネルギーの放出。何かを生み出す人間のもつナマの魅力が十分に伝わってくる。

小高 賢（歌人）

文芸春秋・3000円

■李方子 一韓国人として悔いなく 小田部 雄次〔著〕

宮家から嫁いだ女性の生涯

1910年の韓国併合に伴い、大韓帝国は日本の植民地となった。皇帝は李王と改称され、やがて最後の皇太子だった李垠（り・ぎん）が李王家を継ぐ。本書は、皇族梨本宮家から李垠に嫁ぎ、両国の狭間で生きた李方子（り・まさこ）の生涯を追った評伝である。
皇族に準じる待遇を受けた李王家は経済的には恵まれていたが、方子が歩んだ道は、苦難に満ちていた。日韓融和のシンボルとして日本政府主導で決められた結婚、日本・朝鮮双方からの猜疑に満ちた目、毒殺も噂された長男の死。方子が「悲劇の女王」と称されるゆえんである。
戦後、李王家は廃止され、方子と夫は財産を次々と失い、独立した韓国から入国を拒否されるなど、さらなる困難に直面する。晩年にようやく入国を許された方子は、一韓国人「イ・バンジャ」として福祉事業に余生を捧げ、韓国におけるボランティアの先駆者の一人となる。著者は、そこに人間としての美しさを見いだし、彼女が日韓の橋渡しとしての役割を全うしたと評価している。
彼女の生涯を辿ることで、この100年の日本と朝鮮半島の関わりが見えてくる。日韓の将来を考える上でも、一読の価値がある書である。奈良岡聰智（京都大学准教授）

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■マンハッタンを歩く ピート・ハミル〔著〕

「9・11」で故郷を見つめ直す

著者は新聞記者や作家として、長くマンハッタンで働き暮らす。「運がよければ、たぶんここで死ぬだろう」と言い切る生粋のニューヨーカー。故郷を舞台にした自伝的エッセーには自然に思いがこもる。
マンハッタンの中でもダウンタウンとよばれる南部を歩いて、ブルックリン橋、バッテリー・パーク、トリニティ教会、タイムズ・スクエアなどの歴史に思いをはせる。人物や建築物などについての無数のエピソードは、控えめながら誇らしげでノスタルジアにあふれている。
この本を書くきっかけは01年9月11日の世界貿易センタービル崩壊だった。その朝、「落下したガラスと鋼鉄の衝撃で音の世界は空っぽになった」というすさまじい経験をする。それまで恋愛小説やミステリーなどを発表したが、〝喪失〟後はニューヨークそのものをテーマにするようになったという。もう一度、自分の町を見つめ直したいとの衝動に駆りたてられたのだろう。
本著はマンハッタンのガイドブックとしても最適。生き字引の案内で、〝通〟を自任する人も数々の発見を楽しめ、さらにこの蠱惑的な都会に取りこまれること請け合いだ。

多賀幹子（フリージャーナリスト）

雨沢泰訳、集英社・2415円

■内臓感覚 脳と腸の不思議な関係 福土 審〔著〕

「たかが腸」と言うなかれ

毎朝、通勤電車に乗ろうとすると、おなかがゴロゴロしてきてトイレに行きたくなる。腹痛、冷や汗、動悸が耐えがたく、次第に気持ちも滅入ってくる。消化器科で検査しても、「異常なし。気のせいですよ」で終わってしまう。
こんな過敏性腸症候群と呼ばれる疾患が増えている。背景にストレスがあることがわかってきているが、なぜここまで強烈な身体症状が出るのか。この疾患の第一人者である著者は、臨床データや実験から「脳と腸のあいだにある密接な交流」を明らかにしていく。医学用語も多いが、説明は分かりやすい。腸は自ら受けた刺激を「内臓感覚」として脳に伝え、脳は自律神経やホルモンを介して腸に影響を与える。私たちが意識していなくとも、このような身体からの情報が脳での情動形成にも深くかかわっている可能性もあるのだ。「たかが腸」などと言うなかれ。
過敏性腸症候群は、内臓と脳や心との関係を教えてくれる重要な疾患であるが、それだけに十分な時間をかけた専門的治療が必要になる。ところが、「時間的余裕も経済的裏づけも急速に悪化」しているいまの医療状況ではそれも困難、とする著者の嘆きにも耳を傾けたい。

香山リカ（精神科医）

NHKブックス・1019円

私の読書日記

暴力革命、IBS、高松塚への道

ノンフィクション作家
立花 隆

×月×日

かつてパレスチナに渡り、日本赤軍に合流したこともある若松孝二監督が『実録・連合赤軍――あさま山荘への道程』という三時間十分の長編ドキュメンタリータッチの映画を作った。試写を見た。実写記録と役者を使ったドラマが交錯して不思議なリアリティをかもし出す映画だった。

ドラマ部分はすべて、連合赤軍兵士たちの記録にもとづいているから、実写以上に迫力がある。

はじめは安っぽいドラマに見えたが、みるみる、革命の名の下に犯される凄惨な殺し合いドラマに引き込まれた。驚くべき迫力。

この迫力は、それが本当に起きたことだという事実の持つ重みからきている。

若松監督は、「死ぬ前に、どうしても撮っておきたかったテーマでした」という。この事件の総括なしには現代が見えてこないという。よくぞこれだけ陰惨で重いテーマの映画を作ったものだと思う。

この映画のもとになった史実部分は、ほとんどが、彩流社から出ている連合赤軍幹部と兵士たちの手記をベースにしている。たとえば、坂口弘『あさま山荘1972』（上下巻 各1845円＋税）、永田洋子『十六の墓標』（上下巻 上1500円・下1800円＋税）、植垣康博『兵士たちの連合赤軍』（1800円＋税）などだ。

映画は、「連合赤軍」結成以前のそもそもの「赤軍派」結成前後のあたり（日本赤軍の重信房子もいた頃）から詳しく描いている。

その辺は、赤軍派の創設者、塩見孝也の『赤軍派始末記』（1800円＋税）がいい資料になる。

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連合赤軍事件のみならず、戦前の日本共産党のリンチ殺人事件など、暴力革命路線をとる革命党の内部で、洋の東西を問わず、よく同志殺しが起る。

その手の殺人で歴史上最も有名な事件が、一八六九年、帝政ロシアで起きたネチャーエフ事件だ。

ペテルブルグの大学生だったネチャーエフは、革命のためには、殺人であれ、恐喝であれ、何でも許されると主張する過激派だった。彼は、「民衆の裁き」という名の秘密地下組織を作った。メンバーの一人が組織を裏切る素振りを見せたとき、裏切り者を処刑すれば組織固めになると考えた。実際その男を仲間とともに殺害し、遺体を池に捨てた。

この事件を下敷きに書かれたのが、ドストエフスキーの最高傑作の一つ『悪霊』（新潮文庫 上下巻 上819円・下895円＋税）である。

「アレクサンドルII世暗殺」

このあたりから、ロシアではテロの嵐が吹きすさぶ時代がはじまった。善と悪の境界が取り払われ、革命のため、善のため、真理のためなら殺人が許されると信じるテロリストたちが大挙して出現し、次々と大胆なテロ事件を起こした。

なかでも有名なのが、一八八一年に起きたロシア皇帝アレクサンドル二世の暗殺事件。この事件を詳細に描いたのが、エドワード・ラジンスキー『アレクサンドルII世暗殺』（NHK出版 上下巻 各2300円＋税）。

ネチャーエフ事件も詳しく語られ、それがドストエフスキーの作品をはるかに上まわる悪魔的な事件だったとわかる。読めば読むほど、連合赤軍事件とネチャーエフ事件の共通項が見えてくる。

彼らは一般社会の道徳をいっさい認めない。道徳の唯一の判断基準は、それこそアこれだなと思われる症例が詳しく解説されていた。病名は過敏性腸症候群（IBS）。心因性の病気で、心理的社会的なストレスがいっても、脳に最も近い臓器だからだ。セカンド・ブレインといわれるくらい、本質において脳に近いところがあるから。時に情動作

の大発見といわれた高松塚古墳が、当局の保存策の不手際から、カビだらけになったことだ。その結果、あの貴重な壁画がいまや消え

たちばなたかし　1940年長崎県生まれ。『宇宙からの帰還』『サル学の現在』『シベリア鎮魂歌――香月泰男の世界』『滅びゆく国家』ほか著書多数。

な形し合いドラマに引き込まれた。驚くべき迫力。

この迫力は、それが本当に起きたことだという事実

ーエフ事件の共通項が見えてくる。

彼らは一般社会の道徳をいっさい認めない。道徳の唯一の判断基準は、それによって革命の実現が近づくかどうかである。革命の実現のためには、自ら死ぬ覚悟を持つとともに、革命に有害な人物を自ら抹殺する勇気を持たなければならないとした。

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安倍首相の突然の辞任をめぐっては、何がその真の原因であったか、さまざまの説が駆けめぐった。結局、最大の要因として浮かびあがったのは健康問題。入院した慶應病院の医師の説明では、持病の大腸の慢性疾患がどんどん悪くなり、下痢が止まらず、ものが食べられず、やせる一方だったという。

といっても何らかの感染症にかかっていたわけでもなければ、大腸ガンなどの重大疾患もないという。

福土審『内臓感覚』（NHKブックス　970円＋税）を読んでいたら、ハハアこれだなと思われる症例が詳しく解説されていた。病名は過敏性腸症候群（IBS）。心因性の病気で、心理的社会的なストレスで、腹痛、便通異常（下痢・便秘）が慢性的に持続する。不安・うつなどの神経症状も起きやすい。

まさに安倍前首相の症状にピッタリではないか。

最近欧米の先進国で患者が顕著に増えている病気で、腹部の異常を訴えて医者にかかる患者のうち、平均二〇％はIBSだという。X線検査、血液検査、尿検査などを施しても、特定の病因が見当らないため重大視しない人が多いが、実は大腸の機能不全のうちこれがいちばん多い。

なぜ大腸がこのような心因性の病気にかかりやすいのかといえば、腸は進化論的にいっても、発生学的にいっても、脳に最も近い臓器だからだ。セカンド・ブレインといわれるくらい、本質において脳に近いところがあるから。特に情動作用においては腸が脳に直接働きかけている。

そもそも腸は動物にとって最も大事な臓器。脳がなくても生きられる動物はいるが、あらゆる動物が、腸なしには生きられない。だいたい脳は、腸の神経細胞組織が発達してできたといってもいい臓器。両者の仕組みはよく似ている。腸はいつも脳に神経パルスを送って働きかけているし、脳から腸への信号も常に出ている。腸が心因性の機能不全症を起すことがよくあるのはある意味で当然なのだ。

体質的にIBSにかかりやすい人はどこの国でも一定数いるらしい。しかし、それで総理大臣辞任にまでいたった人が出たのは日本だけらしい。

×月×日

いま思い出しても腹が立つのは、三十五年前、世紀の大発見といわれた高松塚古墳が、当局の保存策の不手際から、カビだらけになったことだ。その結果、あの貴重な壁画がいまや消えたも同然の状態になってしまった。しかも当局がそれをずっと隠蔽してきたため、適切な修復策がこうじられることもなかった。

高松塚古墳の発掘を中心的に行ってきた網干善教氏が生前（昨年死去）語りおろした回想録『高松塚への道』（草思社　1700円＋税）を読むと、その怒りはさらに強まる。

網干氏も、それをずっと何も知らないままできたのだ。三年前はじめて、文化庁監修で出た『国宝高松塚古墳壁画』という一万八千九百円の豪華な図録を見て事実に気がついた。

「僕はページをめくった瞬間、言葉を失いました。鳥肌さえ立ちました。

『これはいったい何やねん』

思わずつぶやいていました。

三十年前、あんなに鮮やかだった白虎の壁画が、ほとんど見る影もなくなって色褪せ、形もよくわからなくなるほど劣化していたのです」

文化庁は、カビが生えた原因を「いわゆる地球温暖化の影響で、気温が三度ほど上がったから」と説明しているが、網干氏にいわせるとぜんぜんちがう。文化庁の純然たるミスである。

高松塚古墳はもともと厚い封土でおおわれ、その上に鬱蒼とした竹藪があった。文化庁はその竹藪を伐採し、封土を全部めくってしまった。

「しかし僕に言わせれば、竹藪を伐採し、土をめくってしまったら、古墳内の温度が上がらないほうがおかしい。担当者は自分たちに都合のいい説明をしているだけ、そしてマスコミは文化庁のその発表を、鵜呑みにしてそのまま書いているだけです」

「文化庁は三十年間、保存のために手を尽くしてきました、一所懸命やってきました、と言う。けれども、じつはまったく何もやってこなかったのではないか」

何もやらないどころか破壊してきたのだ。

【高松塚への道】

植垣康博『兵士たちの連合赤軍』（1800円＋税）などだ。

映画は、「連合赤軍」結成チャーエフ事件だ。

ペテルブルグの大学生だったネチャーエフは、革命のためには、殺人であれ、恐

【アレクサンドルII世暗殺】

フスキーの作品をはるかに上まわる悪魔的な事件だったとわかる。読めば読むほど、連合赤軍事件とネチャ

たちばなたかし
『シベリア鎮魂歌－

『ぼくの血となり肉となった五〇〇冊　そして血にも肉にもならなかった一〇〇冊』が大好評発売中です（小社刊）。この連載の五十回分も収録されています

『私の読書日記』は、立花隆、鹿島茂、池澤夏樹、山崎努、酒井順子の五氏が毎週交代で執筆いたします。