REVIEW

Functional abdominal pain

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Functional abdominal pain or functional abdominal pain syndrome (FAPS) is an uncommon functional gut disorder characterised by chronic or recurrent abdominal pain attributed to the gut but poorly related to gut function. It is associated with abnormal illness behaviour and patients show psychological morbidity that is often minimised or denied in an attempt to discover an organic cause for symptoms. Thus the conventional biomedical approach to the management of such patients is unhelpful and a person's symptom experience is more usefully investigated using a biopsychosocial evaluation, which necessarily entails a multidisciplinary system of healthcare provision. Currently the pathophysiology of the disorder is poorly understood but is most likely to involve a dysfunction of central pain mechanisms either in terms of attentional bias, for example, hypervigilance or a failure of central pain modulation/inhibition. Although modern neurophysiological investigation of patients is promising and may provide important insights into the pathophysiology of FAPS, current clinical management relies on an effective physician-patient relationship in which limits on clinical investigation are set and achievable treatment goals tailored to the patient's needs are pursued.

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Submitted
16 November 2004
Accepted
24 December 2004
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Pain is a symptom commonly reported by most patients with functional gastrointestinal disorders (FGD) and while abdominal pain is the most common symptom in irritable bowel syndrome (IBS) it is associated with other physiological events such as disordered defecation, which is not the case in functional abdominal pain syndrome (FAPS). Hence while the mechanisms of pain in FAPS and other FGDs including IBS are likely to be similar, these mechanisms may not explain the associated disorders of physiological function. To be concise we have focused on the mechanisms of pain in FAPS but the reader should be reassured that similar mechanisms are relevant for understanding pain in other FGDs.

FAPS is one of the less common functional gastrointestinal (GI) disorders occurring in less than 2% of respondents in the US householder study of FGDs compared with 9.2% for IBS.[1]

Despite its relative low prevalence in the community those FAPS patients with refractory symptoms are very likely to be referred to gastroenterology clinics for further (often invasive) investigations, which have to be considered carefully on the basis of both the appropriateness for the person concerned and proper utilisation of healthcare resources.

Diagnostic criteria for FAPS have been defined by the Rome II multiconsensus group and are:
At least six months of:

- Continuous or nearly continuous abdominal pain; and
- No or only occasional relation of pain with physiological events (for example, eating, defecation, or menses); and
- Some loss of daily functioning; and
- The pain is not feigned (for example, malingering); and
- Insufficient criteria for other FGDs that would explain the abdominal pain.[2]

Clearly this classification satisfies the requirement for a uniform study population in clinical and basic research and is not based on any understanding of the mechanisms responsible for symptom generation that remain largely hypothetical.

MECHANISMS OF VISCERAL PAIN PERCEPTION IN HEALTH AND DISEASE

In subjects with functional gastrointestinal disorders including FAPS, an almost universal finding is that they experience more pain in response to an experimental visceral stimulation than normal subjects.[3] [4] This is termed visceral hypersensitivity. To explore this concept we need to understand some basic neurophysiological mechanisms involved in the perception of visceral pain; we will therefore summarise the basic concepts currently considered important.

Pain is a multidimensional experience involving not only an appreciation of the location and severity of noxious stimuli but also evokes an emotional response that might be best thought of as the "suffering" component of pain. Different pain pathways and cerebral regions have been implicated with the pain experience.

Normal visceral pain transduction

To begin let us consider the result of a noxious stimulus within the gut lumen. Our conventional

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understanding is that after activation of peripheral nerve terminal receptors that are sensitive to mechanical, chemical, or inflammatory stimuli (fig 1), the signal is transduced through spinal visceral afferents, which compose 5% to 10% of all fibres in the thoracic and lumbar dorsal roots.[5] These afferents synapse on the dorsal horn of the spinal cord where release of glutamate induces activation of second order spinothalamic neurones via activation of AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazoleproprionic acid) and kainite ligand-gated ion channels.[6] Sensory information is then conducted via the spinothalamic tract (STT), spinoreticular tract, and spinomesencephalic tracts to the brain. The STT terminates in the medial and posterior thalamus and thalamocortical fibres then projects to the primary somato-sensory cortex (SI) and for visceral pain predominately to the secondary somatosensory cortex (SII).[7] This pathway forms the basis of the sensory discriminatory aspect of the pain experience whereas the spinoreticular and spinomesence-phalic pathways eventually terminate on the medial thala-mus and from thence, third order thalamocortical fibres ascend primarily to the anterior cingulate cortex (ACC) and insula; both areas encode the reflexive, motivational, and affective properties of the stimulus with the insula addition-ally involved in the integration of sensory and motor activity (fig 2). Recent evidence suggests the dorsal column that is most commonly known as the conduit of fine touch and vibration stimuli also mediates visceral pain. In a functional MRI experiment Al-Chaer et al[8] have shown that after lesion of the dorsal column at T10 in a primate model of acute visceral pain, brain activation to colorectal distension is greatly attenuated. Interestingly the converse, a lesion in the STT at T10, failed to achieve the same effect.[8 9]

As well as the ascending pathways a number of descending inhibitory pathways play a part in the perception of normal visceral sensation. The origin of the pathways is the opioid rich ACC and from here inhibitory signals are conveyed to the periaqueductal grey either directly or via second order neurones from the amygdala. Other midbrain regions where synaptic connections are made include the locus coeruleus and rostral ventral medulla. Third order opioidergic, serotoninergic and second order noradrenergic neurones connect to the dorsal horn neurones where they "gate" or modulate ascending visceral afferent signals.

This is a simplistic description but is adequate in terms of understanding where abnormalities of pain processing can occur and may contribute to functional abdominal pain.

Abnormal visceral pain perception: the role of peripheral and central sensitisation
Peripheral sensitisation

Studies suggest a third of people after an episode of gastroenteritis will develop IBS and that these people are more likely to show increased levels of mucosal lymphocytes on colonic biopsy compared with controls.[10 11] In addition animal studies, which use models of inflammation, for example GI infection with *Trichinella spiralis*, show that visceral afferent neurones may remain sensitised after the inflammatory insult has elapsed leading to persistent visceral hypersensitivity and intestinal dysmotility.[12]

Modern biological techniques have characterised possible putative receptors on peripheral nerve terminals that encode noxious stimuli and include: sodium channels, for example, SNS1/SNS2; the P2X3 (purinergic) receptor that is sensitive to adenosine triphosphate (ATP); neurokinin receptors, such as NK1; acid sensitive ion channel (ASIC) receptors in particular ASIC 3 and vanilloid receptors, principally TRPV1.[13–16] In inflammatory conditions these receptors' sensitivity is increased by the release of local inflammatory mediators like the prostaglandin PGE_2, bradykinin, neuro-trophins, and cytokines, which can induce increased receptor expression or receptor activation by the removal of local inhibitory mechanisms. For example, after inflammation bradykinin induces activation of protein kinase C (PKC), which in turn leads to sodium channel (SNS) and TRPV1 sensitisation.

The neurotrophic factor, nerve growth factor (NGF) is absorbed by the peripheral nerve terminal and retrogradely transported to the cell body where it induces increased TRPV1 expression, these new receptors are then anterogradely transported to the peripheral terminal.[17]

PGE_2 causes increased cyclic adenosine monophosphate (cAMP) expression via G protein coupled stimulation of adenylate cyclase (AC). cAMP may induce sensitisation by modulation of ion channels, increased receptor expression, or further interactions with secondary messengers, for example, $Ca^{2+18-21}$ (fig 1). Visceral hypersensitivity might therefore be started by an inflammatory event in the gut such as infection or surgery and in susceptible people induce sensitisation of peripheral nerve terminals, known as peripheral sensitisation (PS).

In addition genetic differences in secondary messengers of immune cell activation, for example, G proteins, which are involved in the transduction of signals from about 80% of all
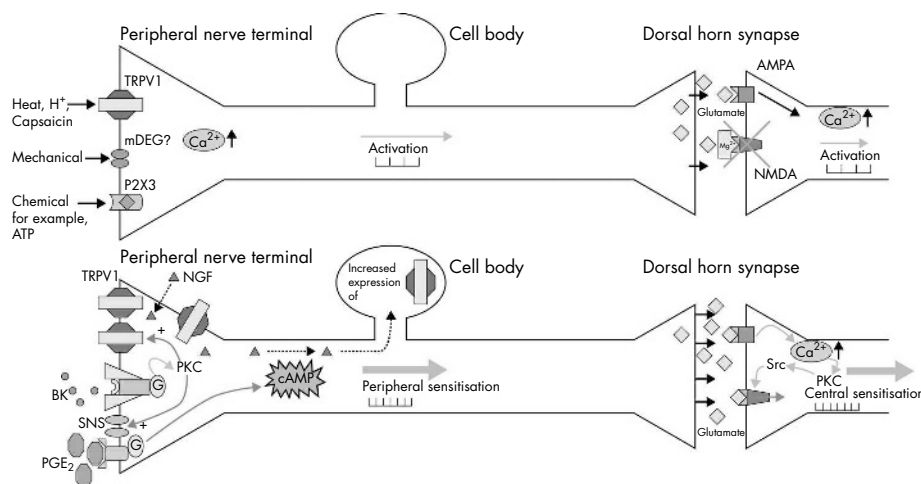

Figure 1 Simplified cartoon showing the major receptor groups and molecular events involved in activation and sensitisation of visceral afferents. (Top) Normal activation. TRPV1, transient receptor potential vanilloid receptor 1 sensitive to H+, noxious heat and capsaicin; mDEG, m Degenerin (a candidate receptor for mechanical transduction); P2X3, purinergic receptor; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazoleprionic acid receptor; NMDA, N-methyl-D-aspartate receptor. (Bottom) Sensitisation. At the dorsal horn synapse increased levels of afferent neurone activation lead to the activation of the NMDA receptor by the removal of the magnesium ion block. BK, bradykinin; PGE_2, prostaglandin E_2; G, G protein; PKC, protein kinase C; Src, tyrosine kinase Src. (See text for more details).

MCC

pACC

SII

Insula

C

Thalamus

Medial lemniscus

Reticulothalamic tract

Spinothalamic tract

Dorsal reticular nucleus

Nucleus gracilis

Spinoreticular tract

Fasciculus gracilis

Dorsal horn neuron

Dorsal column

B

Dorsal root ganglion
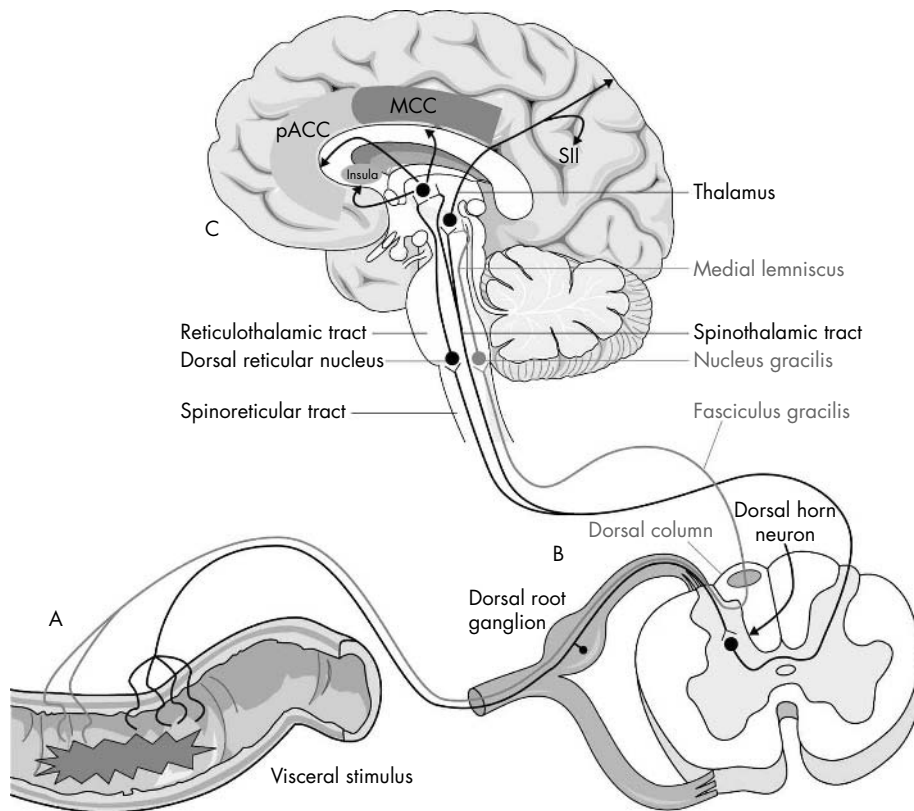
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Visceral stimulus

Figure 2 Simplified diagram showing the major pain pathways from the viscera to the central nervous system. Note the inclusion of the dorsal columns whose role in visceral pain perception is becoming increasingly recognised. pACC, perigenual anterior cingulate cortex; MCC, midcingulate cortex.

cellular membrane receptors, may play a part in determining susceptibility to a gut inflammation. G proteins are essential for stimulus-response coupling of receptors linked to intracellular effector systems such as the adenylcyclases, the phosphoinositide system, ion channels, as well as various protein kinases and transcription factors. A recent study has shown that a polymorphism for the gene GNB3 that encodes the 3 subunit of heterotrimeric G proteins may be increased in patients with functional dyspepsia; the authors speculate that the resultant defective G protein signal transduction in these patients may compromise normal immune cell: pathogen interactions in the gut leading to poor pathogen clearance and susceptibility to FGD. Alternatively compromised G coupled signal transduction might also interfere directly with local inhibitory adrenoceptor nerves and induce visceral hypersensitivity.[22]

Central sensitisation
The increased afferent neurone barrage to the dorsal horn (DH) neurones of the spinal cord because of PS causes central sensitisation (CS) by increased presynaptic glutamate secretion, which leads to the removal of the magnesium ion block of the N-methyl-D-aspartate (NMDA) receptor.[23] Additional key enzymes in the dorsal horn neurone include protein kinase C (PKC) and the tyrosine kinase, Src, which are produced as the end product of the activation of multiple G protein coupled receptors and further contribute to CS by phosphorylation of the NMDA channel. The resulting increased responsiveness of the dorsal horn neurones outlasts the initiating insult and may only require a low level peripheral input to maintain it. In addition the recruitment of surrounding DH neurones, termed heterosynaptic potentiation, makes the area from which the stimulus originated in the gut appear enlarged (see fig 1).

Recently Willert *et al* have shown in healthy volunteers that the NMDA antagonist ketamine can reverse acid induced oesophageal hypersensitivity mediated by CS suggesting a role of the NMDA receptor in human visceral hypersensitivity.[24] Clinical evidence that CS may mediate FAPS comes from studies that show that patients with FGD have an increased likelihood of developing fibromyalgia or to have multiple functional GI syndromes at the same time, or both, for example, functional dyspepsia or non-cardiac chest pain.[25 26] These clinical findings of a ''globally'' sensitised somatic and visceral afferent nervous system suggest CS, occurring at the level of the spinal cord is an important mechanism of viscerosomatic and viscerovisceral sensitisation.[27 28]

THE NEUROPHYSIOLOGICAL INVESTIGATION OF VISCERAL PAIN
Various neurophysiological techniques have been used to explore normal and abnormal pain processing within the central nervous system. Primarily these techniques have focused on the examination of GI afferent pathways and elucidation of the brain areas involved in the cognitive interpretation after a visceral stimulus:

Cortical evoked potentials (CEP)
In this technique an electroencepholagraph (EEG) is recorded during runs of stimulation (usually electrical or mechanical) of the viscera undergoing investigation. Recording of EEG is phase and time locked with the stimulus and after successive stimuli extraction of background randomly occurring EEG waves can be achieved leaving the desired stimulus evoked brain activity. This technique can be used to assess visceral afferent pathway integrity and may give an indication of whether these pathways have been sensitised to promote visceral afferent transmission to the central nervous system.[29–31]

Positron emission tomography (PET)
This cerebral scanning technique permits measurement of cerebral blood flow, a proxy of neuronal activity, after the intravenous injection of a radioisotope, for example, labelled

Table 1 Methods and results of the studies on patients with functional gastrointestinal disorders

Reference	Patients (n)	Normal subjects (n)	GI tract studied	Technique	Principal findings
Furlong et al Neurophysiol[52]	NA		Oesophagus	MEG	Non-painful stimulus with balloon distension caused activation of SI, SII, insular cingulate cortex and the ACC
Aziz et al Gastroenterology[53]	NA		Distal oesophagus	PET	Painful and non-painful stimulation. Inferior border of SI activated with both stimuli. ACC activation with painful stimuli
Silverman et al Gastroenterology[54]			Rectum	PET	Normal subjects: actual or simulated painful stimuli evoked activation of ACC. IBS subjects left prefrontal cortex activated but no ACC activation.
Mertz et al Gastroenterology[55]	18	16	Rectum	fMRI	Normal subjects and IBS showed activation of thalamus, insular cortex, ACC and prefrontal cortex. IBS patients reported greater intensity of pain and had increased ACC activation
Naliboff et al Gastroenterology[56]	42 (IBS) 23 women 19 men	NA	Rectum	PET	Female IBS subjects showed greater activation in the ventromedial prefrontal cortex, right ACC, left amgdala. Male IBS subjects showed increased activation in right dorsolateral prefrontal cortex, insula and PAG. Conclusion: Different sex IBS subjects differ in activation of brain areas after visceral stimulation
Verne et al Pain[57]	9 (IBS)	9	Rectum	fMRI	Rectal distension and somatic heat stimulation compared between IBS and normal controls. Increased neural processing evoked to both stimuli in IBS patients and at different cortical levels, suggesting increased afferent activation, such as, selective aberrant central nervous processing
Phillips et al[34]		8	Oesophagus	fMRI	Study in which oesophageal stimuli where presented with visual stimuli (neutral or fearful faces). Significantly greater oesophageal discomfort and activation of left dorsal anterior cingulated gyri and bilateral anterior insulae occurred with fearful faces

water ($H_2^{15}O$) by the detection of positron emitting radio-nuclides.[32] Block design experiments are used that compare the perfusion images taken when the subject is at rest with those when the subject is experiencing a visceral stimulus.

Functional magnetic resonance imaging (fMRI)
fMRI detects increases in blood flow in areas of heightened neuronal activity by the detection of oxygenated haemoglobin. Paradoxically increased neuronal activity and hence blood flow correlates positively with levels of oxyhaemoglobin, as spurts of neuronal activity are associated with anaerobic brain metabolism. Thus increased oxyhaemoglobin at the sites of increased neuronal activity produces an increased signal that can be interpreted to show the structures activated by the visceral stimulus. fMRI has a superior temporal resolution compared with PET of between four and eight seconds and because no radioisotopes are used permits repeated studies on the same subject.[33]

Magnetoencephalography (MEG)
Visceral stimulation leads to cortical activation that generates minute magnetic fields. These can be detected with highly sensitive sensors known as SQUIDS (super conduction quantum interference device), which are contained within a helmet-like apparatus that covers the subject's head. As well as having comparable spatial resolution to PET and fMRI, MEG has a superior temporal resolution that permits a more dynamic interpretation of brain area activation after visceral stimulation. This latter quality and the technological advances allowing deeper regions of the brain to be studied offer the exciting prospect of providing a second by second evaluation of pain pathway activation and patterns of aberrant pain processing.

The evidence from studies using the above techniques suggests that noxious visceral stimuli produce some differences in cortical activation of the brain than that induced by somatic stimuli. These studies show that cortical processing of visceral sensation entails initial processing in the primary and secondary somatosensory cortices (for sensory discrimination), with subsequent involvement of the anterior cingulate (ACC) and pre-frontal cortices for affect and cognition respectively. This shows that it is possible not only to localise the site of our gut sensation but it is also possible to assign emotional value to it. Furthermore, the study by Phillips et al[34] is of particular relevance to FAPS as it shows that even in normal subjects, visceral stimuli presented within a negative emotional context (that is, oesophageal stimuli presented at a time when subjects were viewing fearful facial expressions on a screen) are rated as more unpleasant and cause significantly more activation of brain areas involved in cognitive pain processing than those stimuli paired with neutral faces. This suggests that the psychological state of the person plays an important part on visceral sensory perception and the brain processing.

Studies have also shown that patients with functional gastrointestinal disorders either display an increased activation in brain areas involved in processing visceral sensation or show different areas of cortical activation than control subjects. However, these studies are preliminary and do not shed light on specific pathophysiological mechanisms of heightened pain perception in patients with functional gastrointestinal disorders. (For a detailed review of the literature on functional brain imaging in functional gastrointestinal disorders please see Hobson and Aziz[35]).

Table 1 describes the results of such studies and the method used in each.

Therefore in summary the mechanisms involved in symptom production in FAPS and other functional digestive disorders are potentially multiple and interconnected. The scientific challenge will be to correctly interpret the results of studies, in the knowledge that no method is without its

limitations, to produce an organised objective understanding of different phenotypes within this heterogeneous population and from thence to evaluate the potential genetic susceptibilities responsible for them.

CLINICAL EVALUATION OF THE FAPS PATIENT
History
The initial evaluation of FAPS patients in primary and secondary care should be essentially the same and begins when the patient enters the consulting room. A careful history should be taken that takes into account not only the chronology of pain events, for example, relation to surgery or adverse or traumatic life events but attention should be paid to the emphasis and style with that these are described by the patient. Pain is often described by patients in more emotional terms than those with structural disease with terms like ''agonising'' and ''sickening'' rather than crampy, sharp, or stabbing. In addition, abdominal pain often covers a large area and may be one of several pains suffered by the patient suggesting concurrent somatisation disorder. The intensity of abdominal pain seldom varies with maximal pain being experienced most of the time, which contrasts with structural disease in which the pain intensity varies and is also more likely to affect other GI activity, for example, motility.

Some behaviour traits may come to light during a consultation that might lend weight to a diagnosis of FAPS. These would include reluctance on the part of the patient to consider the contribution of psychosocial factors to their symptoms and a reliance on invasive investigation to discover an organic cause for the symptoms. Health seeking behaviour is increased in FAPS patients as is the demand for ever increasing analgesia.[36]

Although the above description may be reasonably typical of FAPS patients, it should be emphasised that all patients, whatever the aetiology of their pain are apt to describe their symptoms in more or less dramatic terms and this should be considered in the context of the whole evaluation.

Physical examination
While characteristically examination in a FAPS patient should fail to discover abnormality, several features should be noted, for example, the absence of autonomic arousal, presence of abdominal scars, and closed eyes sign[37]; in which the subject closes their eyes during examination, which is the

opposite of the more fearful anticipation displayed by sufferers of an acute abdomen.

Distraction can be used with a stethoscope pressing with firm pressure on the abdomen when previously the examining hand may have elicited pain at the same spot. Finally Carnett's test may be performed, in which a painful area is palpated before and after the patient tenses his abdomen by essentially performing a sit up against the resistance of the examiners hand on the subject's forehead. If the subject experiences pain with palpation against tense abdominal musculature, this suggests the cause of the pain is not intra-abdominal and may be musculoskeletal in nature.[38]

Investigation
A limited investigation may be warranted in selected cases and could include screening laboratory studies, for example, full blood count, erythrocyte sedimentation rate, serum biochemistry, and C reactive protein. In those patients in which alarm features such as rectal bleeding, weight loss, or anorexia are present then another diagnosis should be considered and investigated accordingly. Naturally secondary care providers will feel under pressure to provide endoscopic investigation by both the virtue of ease of access to endoscopy within a district general hospital and the FAPS patient's reliance on such procedures to provide reassurance and explanation to their symptoms. Another cause of worry is the possibility of missing structural disease especially cancer. Several retrospective and prospective studies suggest that diagnostic failures occur in only 0% to 4.5% and this should be borne in mind in the follow up of such patients especially if symptoms change.[39 40]

Management
Several aspects of management are worth clarifying. Patients should be provided with a positive diagnosis of their condition and a full explanation of the diagnosis in an acceptable manner that takes into account their belief system.[2] This should include a general description that FAPS is a disorder with multiple causes that vary patient to patient, and that the mechanism of symptom generation is not fully understood, but is most probably attributable to a disorder of pain processing and modulation.

It is important to ensure that the patient is aware that an outright cure is unlikely and that the mainstay of treatment is aimed at symptom control. Tricyclic antidepressants (TCA) are widely used in the management of FGDs and are prescribed a low dose, for example, amitriptyline 25 mg once daily. Proposed mechanisms of action include antagonism of the NMDA receptor where they bind and reduce the intracellular accumulation of calcium in spinal neurones and possibly directly via inhibition of Na^+ and K^+ channels.[41 42] Low dose TCA are preferred as higher doses lead to sedation and may lead to patient non-compliance and also effective doses are seldom reflected in higher serum concentrations, suggesting that low dose is sufficient for TCA to work as CNS analgesics rather than antidepressants.[43] Conversely the results of (IBS) studies with selective serotonin reuptake inhibitors (SSRIs) have been conflicting and therefore SSRIs are of uncertain benefit for FAPS patients.[43] However, some authorities suggest using a dose of fluoxetine 20 mg in isolation or lower doses in combination with TCA in selected patients in whom anxiolysis or control of significant concurrent psychological problems is required.[36 43–45]

Narcotic drug treatment is best avoided as opioid gut receptor stimulation eventually leads to opioid receptor down regulation and reduced gut motility—that is, the narcotic bowel syndrome.[2]

> **Key points**
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> - Functional abdominal pain syndrome (FAPS) is one of the functional gastrointestinal disorders (FGD) defined as abdominal pain in the absence of an identifiable disorder.
> - FAPS patients are a heterogeneous group whose symptoms are likely to be attributable to multiple causes.
> - Disorders of pain processing that include peripheral and central sensitisation, defective descending modulation of afferent pain pathways, and hypervigilance towards normal visceral sensations are likely to be involved in the initiation and maintenance of FAPS.
> - Clinical management should include a thorough history including a comprehensive account of psychosocial problems and limited investigations.
> - Treatment options include low dose tricyclic antidepressants and psychological approaches, for example, cognitive behavioural therapies.

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More resistant cases might benefit from psychological treatments.

Cognitive therapy

In cognitive therapy, patients are encouraged to explore the maladaptive beliefs about their pain and are encouraged to re-conceptualise their pain and take a more active role in its management. Keeping a diary record with pain sampling taken throughout the day will show the relative variability of symptoms and their association with anxiety or stress that may have accompanied the pain experience.[46] Therapy is directed at helping the patient to develop an understanding of the interdependent aspects of the pain experience and to use coping strategies that tackle the pain experience in terms of its effect on daily functioning, for example, social, recreational, and financial repercussions. Rather than "curing the pain", treatment goals should be realistic and include short, medium, and long term objectives that help the patient perform their daily activities to their full potential. Available evidence suggests that cognitive therapy is efficacious with almost twice the response rate compared with providing the patient with just information on their disorder.[47]

Behavioural therapies

Therapy is aimed at increasing activities in a graded way without necessarily involving the self analytical approach detailed above. The emphasis here is on ignoring pain and reinforcing activity related behaviour. Biofeedback has a limited role (if at all) but relaxation and stress management techniques may be useful as part of a behavioural therapy programme.[48]

Hypnosis

This is perhaps a marginalised area of functional gut disorder research and most of the available evidence pertains to IBS patients. Hypnosis is used to induce general relaxation and also suggestions are made whereby patients are encouraged to use imagery or visualisation in an attempt to assert control over gut sensation/function. Hypnotherapy leads to improved clinical outcomes but also improvements in physiological markers are seen, for example, rectal sensitivity to balloon distension are seen to normalise after hypnotherapy in IBS subjects with reported rectal hypersensitivity.[49 50]

What remains to be seen is the objective effect of hypnosis in the modulation of visceral pain. Recent evidence from an fMRI study of normal subjects hypnotically induced to feel a somatic thermal pain stimulus showed activation within the thalamus, ACC, and insula cortex of greater magnitude than a control group who were requested to recall a previously experienced somatic pain stimulus. This suggests that activation of certain cortical structures can induce pain regardless of peripheral input and may be of great relevance to the cause or continued symptoms experienced by FGD patients.[51] The results of similar imaging studies with visceral stimuli in normal and patient populations are eagerly awaited.

Summary

Patients with FAPS form a comparatively small part of the FGD population but present a difficult diagnostic and management problem to the clinician. In contrast with previously held beliefs it is better to consider FAPS in the context of the whole organism by adopting the broader perspective of the biopsychosocial model rather than the more reductionist biomedical model. This requires patience, persistence, and the help of multiple disciplines within primary care and secondary care. Drug treatment options are limited and include TCA and possibly the newer SSRIs but both are probably of little use in more chronic cases without an organised psychological treatment programme.

The elucidation of the mechanisms underlying functional digestive disorders is an exciting area of gastroenterology research and no doubt the solution will be as complex as the problem. FAPS patients represent a heterogeneous group with multiple mechanisms responsible for the initiation and maintenance of symptoms. Therefore the correct identification of these subgroups remains a priority both to clinicians and scientists. Modern imaging and molecular techniques offer the tools for the elucidation of these mechanisms by identification of central nervous system pathways that have undergone sensitisation and modification. Future treatments may entail the activation or attenuation of putative receptors within the GI tract, for example, TRPV1 antagonists; spinal cord or brain, for example, NMDA antagonists, which are felt to contribute significantly to symptom production. Furthermore, pharmacogenetics may help to identify those patients with susceptibility to developing FAPS and also those most likely to respond to the above treatments.

MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AT END OF REFERENCES)

1. True or false

(A) Functional abdominal pain syndrome occurs in about 5% of the population.

(B) FAPS patients quite often feign symptoms to obtain secondary benefit.

(C) Visceral hypersensitivity may be an important physiological finding in determining the cause of FAPS symptoms.

(D) Visceral pain is transduced in exactly the same pathways as somatic pain.

(E) Central sensitisation can occur at the level of the dorsal horn by the reversal of the magnesium block of the AMPA receptor.

2. Concerning normal visceral pain transduction

(A) Most painful visceral sensations are conducted to the central nervous system via the vagus nerve.

(B) TRPV1 receptors are activated by protons or capsaicin and cause a characteristic burning sensation.

(C) Second order spinothalamic neurones are stimulated via activation of AMPA receptors.

(D) Glutamate is the major excitatory signalling peptide at the dorsal horn synapse.

(E) Serotoninergic and noradrenergic neurones are involved in modulating ascending visceral afferent signals at the level of the dorsal horn.

3. Regarding peripheral sensitisation

(A) A history of gastroenteritis may be reported in up to two thirds of IBS patients

(B) During inflammation NGF release increases TRPV1 expression in the neurone cell body.

(C) Increased levels of c AMP may be responsible for afferent neurone sensitisation.

(D) Animal models of GI inflammation often use nematode infections to simulate short lived inflammation.

(E) G protein polymorphisms may be increased in functional gastrointestinal disorders leading to immune cell dysfunction.

4. Regarding functional neuroimaging in FGD studies

(A) PET is an imaging modality that is ideal for repeated scanning of study subjects

(B) MEG has a superior temporal resolution in comparison with fMRI.

(C) Visceral stimuli paired with negative emotional visual stimuli cause greater activation of brain areas involved with processing cognitive aspects of the pain experience.

(D) Increased activation of brain areas on fMRI is analogous with increased levels of oxyhaemoglobin at these sites.

(E) The somatosensory cortices are involved with sensory discrimination of painful stimuli whereas the anterior cingulate and pre-frontal cortices are involved in affect and cognitive processing of visceral pain.

5. Concerning the clinical management of FAPS

(A) A history of previous abdominal surgery may be relevant

(B) Extensive GI investigation is warranted in all cases.

(C) Carnett's test may be useful in discriminating between musculoskeletal pain and visceral pain.

(D) A trial of high dose tricyclic antidepressants should be used in most cases.

(E) Studies of cognitive therapy and hypnosis suggest these therapies are of no benefit in patients with FGDs.

ACKNOWLEDGEMENTS

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ANSWERS

1. (A) F, (B) F,(C) T, (D) F, (E) F; 2. (A) F, (B) T, (C) T, (D) T, (E) T; 3. (A) F, (B) T, (C) T, (D) T, (E) T; 4. (A) F, (B) T, (C) T, (D) T, (E) T; 5. (A) T, (B) F, (C) T, (D) F, (E) F.