

Centrally mediated abdominal pain syndromes

Peter Paine

Abstract

Centrally mediated abdominal pain and the associated narcotic bowel syndrome are functional bowel disorders that are challenging to manage and associated with significant medical harm, including unnecessary investigations, opioids and surgeries. They are distinguished from more common conditions, such as irritable bowel syndrome, by the near-continuous nature of the pain, irrespective of gastrointestinal physiological functioning. Their pathophysiology is obscure and incompletely understood, but they have features consistent with central sensitization. Long-term opioid use can cause hyperalgesia and dysmotility, leading to a vicious cycle of increasing healthcare use and breakdown in the doctor–patient relationship. Gut–brain neuromodulatory drugs, along with a holistic rehabilitative multidisciplinary approach, patient education and opioid detoxification, can lead to improved outcomes.

Keywords Centrally mediated pain; gut–brain neuromodulators; iatrogenesis; MRCP; narcotic bowel syndrome; opioids

Introduction

The Rome IV diagnostic criteria of functional gastrointestinal disorders (FGIDs) have recently included centrally mediated abdominal pain syndrome (CAPS) and narcotic bowel syndrome (NBS). These disorders are now recognized in their own right as being related to each other but distinct from other more established disorders, such as irritable bowel syndrome.¹ Nobody knows exactly how common they are (prevalence estimates 0.5–2%, more common in women), and they are thought to peak in the mid-30s to early 40s.

Although the pathophysiology of these disorders is incompletely understood, it has been postulated that they arise from abnormal processing of pain signals within the central nervous system, hence the current nomenclature of ‘centrally mediated’. In the previous diagnostic Rome (III) criteria, CAPS was referred to as ‘functional abdominal pain syndrome’. It was speculated that this might be a type of neuropathic pain, and it certainly shares some clinical features of neuropathic pain, including allodynia (non-painful stimuli perceived as painful),

Peter Paine MBBS MRCP PhD is a Consultant Gastroenterologist at Salford Royal Foundation Trust, UK, running a regional tertiary neurogastroenterology clinic, and has a special interest in chronic abdominal pain. He is currently the Chair of the Neurogastroenterology and Motility Section of the British Society of Gastroenterology. Competing interests: none declared.

Key points

- The cause of chronic continuous abdominal pain may lie in the central pain system ‘wiring’ rather than the end-organ ‘plumbing’
- Avoid opioids for this condition as they will almost certainly make things worse
- Avoid surgery for these patients, including for adhesions not threatening bowel viability, as this also usually worsens outcomes
- Gut–brain neuromodulators and a holistic multidisciplinary approach are key to better outcomes

hyperalgesia (painful stimuli perceived as more painful) and a constant and spontaneous nature.²

There is mounting evidence that opioids can alter the neurobiology of pain processing in already sensitized nerves, through multiple molecular mechanisms, resulting in ‘opioid-induced hyperalgesia’. This is a counterintuitive concept in that the opioids are making the pain more painful. This has, however, been confirmed, in that carefully stopping opioids can result in an overall reduction of pain levels.³

Diagnosis

History

On assessing the history, the hallmark of CAPS is the nearly constant nature of the abdominal pain. This distinguishes it from the episodic and intermittent nature of the other painful FGIDs, which are also usually associated with gastrointestinal (GI) physiological events, such as defaecation or eating. Although centrally mediated pain sometimes worsens with physiological GI events, the pain is nonetheless present and continuous irrespective of GI function. Similarly, GI function can also be impaired, but the pain is the overriding and predominant feature. The history of the pain characteristics is therefore the main clue to the diagnosis.

There is sometimes a clear trigger for the onset of the pain (e.g. after an operation or severe infection), but more commonly there is no clear trigger. There can also be a concomitant history of other chronic painful conditions such as fibromyalgia, or other medically unexplained disorders. It is very common for patients to be psychosocially distressed with poor quality of life and poor levels of functioning.

A history of analgesic use, especially opioid dose, frequency and route of administration, should be elicited. Evidence of dose escalation, chaotic use and emergency department attendance for opioid injections should also be noted.

The characteristic of NBS is the vicious cycle of escalating doses of opioids, in tandem with escalating pain levels. This is known as the ‘soar and crash’ phenomenon (Figure 1), and

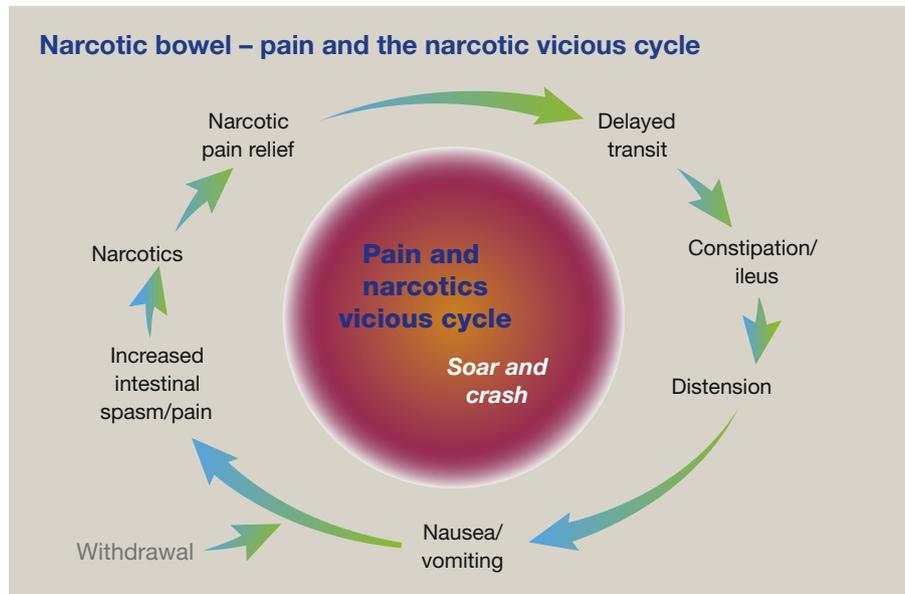


Figure 1

involves: (1) short-lived temporary relief with dose escalation (often simply caused by dissociative narcosis); (2) short-term symptom worsening if doses decrease, because of opioid withdrawal; and (3) background chronic worsening of gut function and pain.

'Yellow flags' are psychosocial indicators suggesting an increased risk of progression to long-term distress, disability and potential drug misuse. They include the patient's attitudes and beliefs, emotions, behaviours and family and workplace factors, which should all be sought.⁴

Examination

Some patients find that a hot water bottle gives them some pain relief, so erythema ab igne can be a physical finding on inspection of the abdomen. The presence of surgical scars and their proximity to maximal sites of pain should be determined.

Carnett's sign (Figure 2) is very focal pain on palpation alongside the rectus sheath, which worsens with head or leg raising. This is a sign of the anterior cutaneous nerve entrapment syndrome and should be sought during the examination. Although this can also have some neuropathic features, its more peripheral pathophysiology, caused by localized entrapment of the thoracic intercostal nerves, lends itself to more localized treatment with corticosteroid and local anaesthetic injections; it is therefore an important differential diagnosis to exclude.

Positive clinical findings can include cutaneous allodynia to light touch of the abdominal skin; this is possibly caused by sensitization of the affected dermatome, via viscerosomatic convergence at the level of the spinal dorsal horn (Figure 3). Other abdominal skin sensory changes suggestive of a neuropathic/central sensitized component include dysaesthesia (tingling, numbness).² The abdominal examination should otherwise be normal.

Investigations

Normal investigations are the hallmark of centrally mediated pain, and iatrogenesis caused by continuing futile cycles of

repeated investigations should be avoided. Nonetheless, normal cross-sectional imaging using computed tomography should be sought if not already performed, and normal levels of inflammatory markers, full blood count, liver enzymes and urea and electrolytes should be confirmed.

Patients may have had previous imaging suggestive of adhesional impingement on the bowel. Although adhesions can be associated with episodic exacerbations of pain, they would not be considered a cause of chronic continuous pain. Outside the context of acute obstruction from an adhesion threatening bowel viability, intervention for adhesions is usually counterproductive and associated with worsening pain and greater morbidity.

Similarly, if pain is chronic and continuous with little relationship to menses, endometriosis is not likely to be a major factor; repeated surgical investigations and interventions for this are again likely to be counterproductive. Repeated diagnostic and therapeutic laparoscopies are also therefore to be discouraged.

Management

The optimal approach to management has been summarized by the four Rs: Recognition, Relationship, Replacement and Reduction.

Recognition

A shared recognition with the patient of the features of CAPS and NBS is essential. A positive and clear diagnosis, based on the presence of characteristic features, is key to gaining the patient's confidence in engaging with the therapeutic approach, and avoiding futile or harmful investigations and interventions. It is therefore necessary to spell out to the patient the key features they are exhibiting, and often provide some education on the nature of the 'wiring' of the abdomen and central nervous pain system – some simple wiring diagrams can help in this respect (Figure 3). The counterintuitive and counterproductive effects of opioids also need recognition, with a further clear and careful explanation.

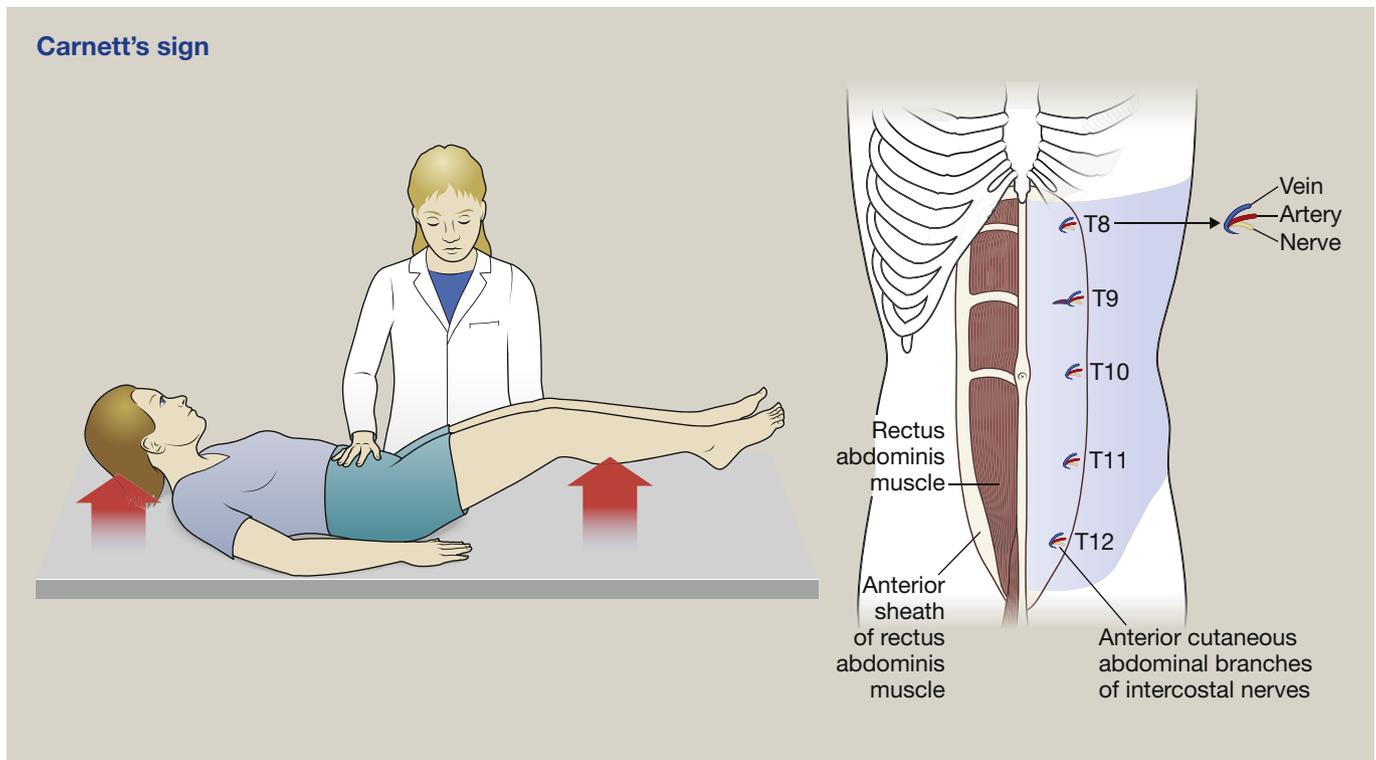


Figure 2

Relationship

This is a chronic condition that is very distressing for patients. They have often had a long period of very negative interactions with healthcare systems and professionals, and there is therefore no substitute for establishing a therapeutic relationship of trust with the patient. The main factors here are time and empathy. It

will take significantly longer than the average consultation to build a rapport and to carefully characterize and disentangle the clinical features and multiple dead ends the patient has hitherto pursued. They may also have encountered many negative responses from other healthcare professionals in terms of the normal test results they have had and the increasing doses of narcotics that are frequently prescribed.

Because these patients are often distressed and disabled, the optimal approach is to build the relationship with a multidisciplinary team (MDT), including pain physicians, clinical psychologists and physical therapists in addition to gastroenterologists. Pain psychology approaches, within a holistic and rehabilitative focused pain management programme aiming to improve function in the face of continuing pain symptoms, hold the best promise of avoiding an increasing spiral of worsening disability.⁴ Effective working relationships and communication with other professionals, to avoid unnecessary further tests and interventions, is also paramount. As patients have often had many years of unhelpful interactions before diagnosis, they are likely to need many years of continuing support for stabilization and progress.

Replacement

Realistic goal-setting includes acknowledging that pharmacotherapy might be of only limited efficacy. Nonetheless, gut-brain neuromodulators, which include many drugs familiar to chronic pain teams for neuropathic pain, can have a role in replacing opioids. These include tricyclic antidepressants, $\alpha_2\delta$ ligands (gabapentin, pregabalin), and serotonin and norepinephrine reuptake inhibitors, such as duloxetine.⁵ There might be a role for

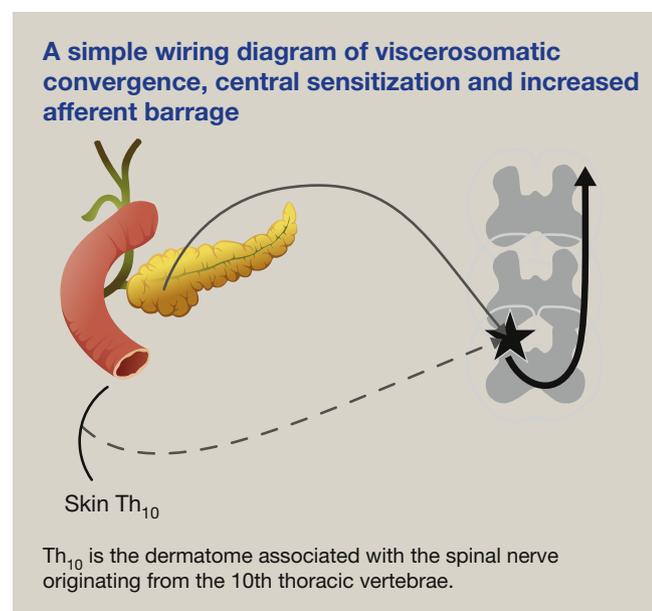


Figure 3

the drug linaclotide, in helping pain as well as gut function, but this remains to be established. The role of atypical antipsychotics (such as quetiapine) as ‘augmenting agents’ in combination with the other gut–brain neuromodulators is also currently less well established, but these can be considered. In most cases, it is in the patient’s best interests to be referred to the chronic pain service on an outpatient basis to help both with pharmacotherapy and an MDT approach.

Reduction

Reduction of opioids can only be realistically considered within the context of a shared recognition with the patient of their maladaptive role, an established MDT relationship of trust, an exploration of replacement gut–brain neuromodulator pharmacotherapies, and holistic rehabilitative focused care.

The first step is rationalization and stabilization of the current opioids to a non-escalating dose, a longer acting formulation and a non-injected route of administration. For more chaotic and frequent emergency department attendees, this can initially require some tight boundaries to be drawn up in conjunction with emergency department physicians and the patient’s general practitioner, with a clearly documented approach to which the patient is made party. This will outline that, in the absence of new acute pathology, injected opioids and opioid escalation will not be supported with signposting back to the chronic pain team in the outpatient setting.

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 37-year-old woman had presented on numerous occasions with a variety of gastrointestinal symptoms. These included continuous abdominal pain, constipation, bloating and sub-sternal burning. She had had numerous investigations, including a diagnostic laparotomy, all of which were normal. Relationships with several doctors had broken down.

Which one of these features is most suggestive of centrally mediated abdominal pain syndrome?

- A Continuous abdominal pain
- B Constipation
- C Negative investigations
- D Previous surgery
- E Relationship breakdown with doctors

Question 2

A 19-year-old woman presented repeatedly at A&E requesting stronger pain relief. She had had a cholecystectomy several months earlier. She was being managed as having narcotic bowel syndrome?

Once stabilized, the most likely long-term prospect of successful opioid reduction is with optimal patient engagement, MDT support and a slow controlled reduction over time to avoid withdrawal adverse effects. Rapid inpatient opioid detoxification is unfortunately associated with very high relapse rates despite initially improved pain symptoms.³ ◆

KEY REFERENCES

- 1 Keefer L, Drossman DA, Guthrie E, et al. Centrally mediated disorders of gastrointestinal pain. *Gastroenterol* 2016; **150**: 1408–19.
- 2 Searle RD, Howell SJ, Bennett MI. Diagnosing postoperative neuropathic pain: a Delphi survey. *Br J Anaesth* 2012; **109**: 240–4.
- 3 Szigethy E, Knisely M, Drossman D. Opioid misuse in gastroenterology and non-opioid management of abdominal pain. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 168–80.
- 4 Keefer L, Mandal S. The potential role of behavioral therapies in the management of centrally mediated abdominal pain. *Neuro-gastroenterol Motil* 2015; **27**: 313–23.
- 5 Drossman DA, Tack J, Ford AC, et al. Neuromodulators for functional gastrointestinal disorders (disorders of gut-brain interaction): a Rome Foundation working team report. *Gastroenterol* 2018; **154**: 1140–71.

What feature would suggest an alternative diagnosis?

- A. ‘Soar and crash’ phenomenon
- B. Escalating opioid use
- C. Demanding the intravenous route
- D. Nausea and vomiting
- E. A rising alkaline phosphatase

Question 3

A 25-year-old man presented repeatedly with continuous abdominal pain, constipation and occasional vomiting. He had a past history of an appendix abscess treated surgically. He was taking increasing doses of tramadol without relief. Clinical examination was normal apart from the scar.

What is the best treatment for the most likely diagnosis?

- A. Advise stronger opioids
- B. Surgical removal of adhesions
- C. Local anaesthetic injection in the rectus sheath
- D. Tell the patient the pain is all in their mind
- E. Clinical psychology