Beyond Fiber and Probiotics: Optimizing Recurrent Abdominal Pain Treatment by Interrupting Visceral Spasm and Hypersensitivity

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Introduction and Epidemiology

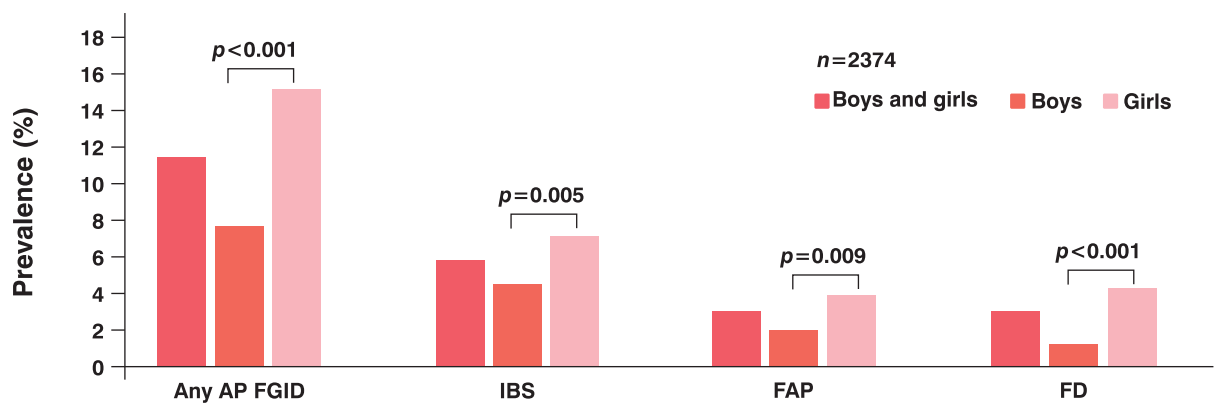
Recurrent Abdominal Pain (RAP) is a prevalent and burdensome condition affecting both children and adults, representing a key component of Functional Gastrointestinal Disorders (FGIDs). It is classically defined as 3 or more episodes of abdominal pain over 3 months that interfere with normal activities Its estimated prevalence is 13–20% in school aged children and up to 15% in adults, underscoring its global clinical significance.[1] RAP contributes significantly to pediatric consultations, frequent diagnostic investigations, and contributes to school absenteeism and diminished quality of life for affected individuals and their families.[2] Long term follow up studies show persistence of symptoms into adolescence and adulthood, often evolving into abdominal-pain-related FGIDs such as Irritable Bowel Syndrome (IBS) (Fig. 4).[1]

Traditional therapies, including reassurance, dietary fibre supplementation, probiotics, and lifestyle modification, show limited and inconsistent success. Emerging insights from neurogastroenterology suggest that RAP involves biological mechanisms such as visceral hypersensitivity, altered gastrointestinal motility, and smooth muscle spasm, all mediated through dysregulation of the brain gut axis. This evolving understanding reframes RAP as a condition rooted in measurable visceral dysfunction rather than a purely psychosomatic disorder.[2]

Pathophysiology of Recurrent Abdominal Pain

Functional Abdominal Pain Disorders (FAPDs) in children are multifactorial, arising from interactions among the Gastro-intestinal Tract (GIT), Central Nervous System (CNS), immune system, intestinal microbiota, and psychosocial factors. A biopsychosocial and neuroimmune microbiota model in pediatric populations, with recurrent pain arising from dynamic interactions between motility disturbances, visceral hypersensitivity, immune dysregulation, and psychosocial stressors.[3,4]

Figure 4: Prevalence of Abdominal Pain Related FGIDs in Children



Visceral Spasm: A Key Driver of Pain and Gut Brain Microbiota Integration

The microbiota intestine brain axis is central to FAPDs, integrating sensory, motor, immune, and cognitive signals between the GIT and CNS (Fig. 5). Direct neural connections, particularly via the myenteric plexus, modulate motility, secretion, and visceral perception, while bidirectional communication allows CNS signals to influence gastrointestinal function. [3,4]

A major driver of pain is visceral spasm, caused by uncoordinated contraction of intestinal smooth muscle triggered by calcium influx and altered cyclic nucleotide signaling via Phosphodiesterase (PDE) regulation. These disruptions cause abnormal transit and delayed gastric emptying, often observed in pediatric IBS and functional dyspepsia. [3]

Clinically, spasms produce colicky, cramp like pain due to increased intraluminal pressure and activation of local nociceptors. Repeated spasm generates persistent nociceptive input, promoting central sensitization and chronicity of pain.

Visceral Hypersensitivity and the Gut Brain Axis

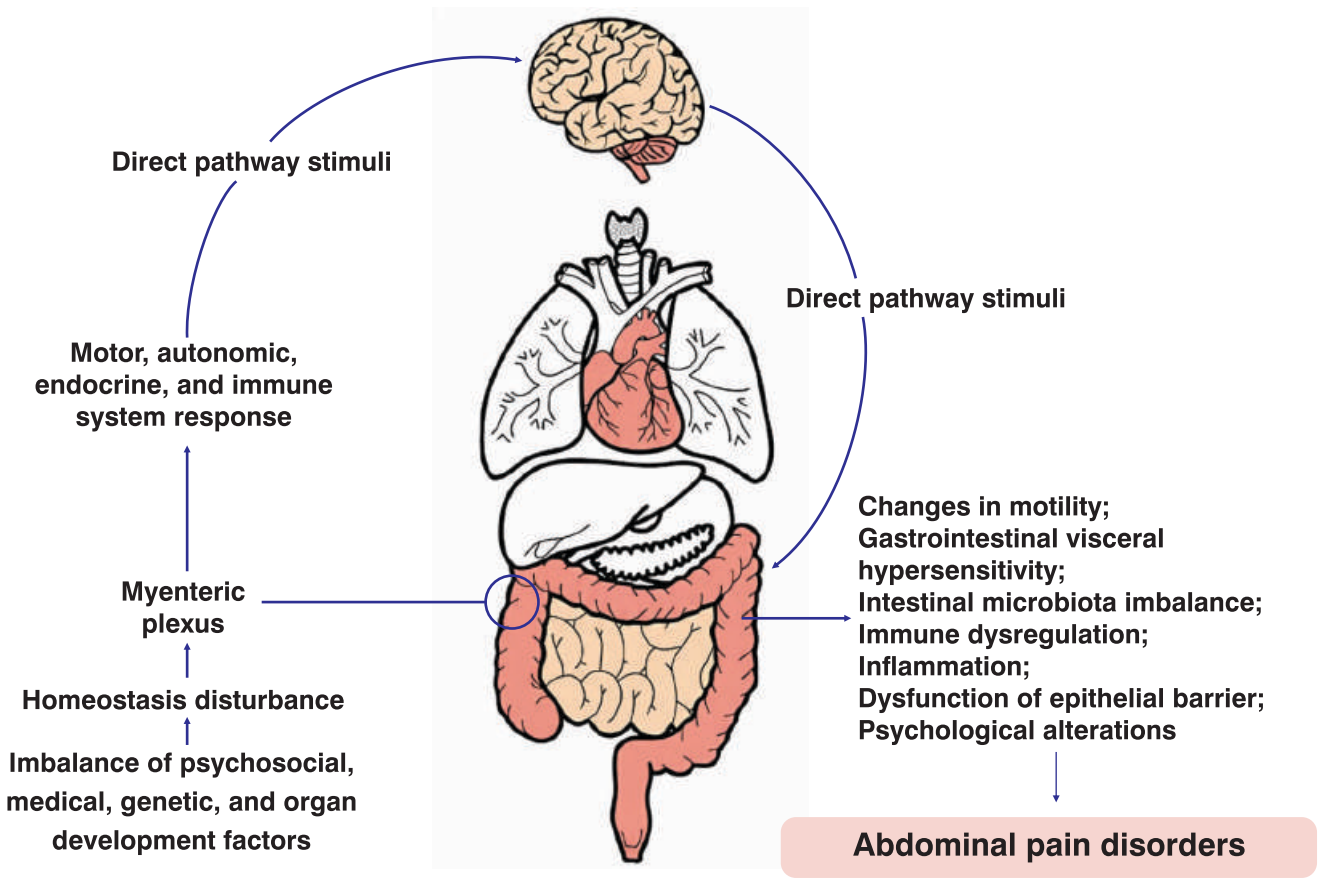
Visceral hypersensitivity is the core mechanism underlying recurrent abdominal pain in pediatric FAPDs. It reflects enhanced neuronal signaling from the enteric nervous system to the CNS, leading to amplified pain perception even in response to normal gut stimuli. [3,4]

Key mediators include:

- TRPV1 receptor activation heightening nociception.
- Serotonin (5-HT) dysregulation affecting motility and sensitivity.
- Mast cell mediators (histamine, tryptase) sensitizing enteric nerves.
- Central and peripheral sensitization, exaggerating normal visceral sensations.

Children with FAPDs show reduced sensory thresholds, suggesting altered processing across the gut brain pathway from the mucosa and spinal cord to cortical centers. Psychological stress and anxiety intensify symptoms via Hypothalamic Pituitary Adrenal (HPA) axis activation, increasing cortisol and cytokine release that influence motility and perception.

Figure 5: Schematic Representation of the Gut Brain Microbiota Axis in FAPDs



Interplay Between Spasm, Hypersensitivity, Microbiota, and Psychosocial Factors

Recurrent abdominal pain reflects a self sustaining cycle:

1. Visceral spasm increases intraluminal pressure → nociceptive signaling.
2. Enhanced pain perception via visceral hypersensitivity and central sensitization.
3. Neural plasticity reinforces hypersensitivity, predisposing to further spasm.
4. Cycle perpetuation leads to recurrent abdominal pain episodes.

This process is influenced by immune and microbiota factors:

Microbiota imbalance further modulates this loop. Children with FAPDs often show increased *Enterobacteriaceae, Lactobacillaceae,* and *Bacteroides,* with reduced *Bifidobacterium and Faecalibacterium* spp., promoting immune dysregulation, barrier dysfunction, and mast cell driven inflammation (Santos *et al.,* 2022). Compromised mucosal integrity facilitates bacterial overgrowth and chronic low grade inflammation.

Psychosocial and dietary stressors (e.g., anxiety, depression, food intolerance) aggravate the cycle through the HPA axis, modulating cortisol and cytokine release, gut motility, and pain perception.[3,4]

Limitations of Conventional Therapy

Fiber and Probiotics

Dietary interventions remain a common first line approach in pediatric FAPDs to improve gut motility and reduce pain. Water soluble fibres such as psyllium, glucomannan, partially hydrolyzed guar gum, and corn fibre increase faecal bulk and may accelerate intestinal transit. Probiotics, particularly *Lactobacillus rhamnosus* GG and *Lactobacillus reuteri,* show some efficacy in reducing pain episodes and improving comfort, while evidence for synbiotics remains inconclusive. Both fibres and probiotics are safe but largely symptomatic relief, as they do not address the core neurogastrointestinal mechanisms. Many children continue to experience persistent pain, underscoring the multifactorial nature of FAPDs, which are not purely microbiota driven.[5]

Need for Mechanism Based Treatment

Given the limited benefit of dietary therapies, management should shift toward mechanism based treatments targeting visceral hypersensitivity, dysmotility, immune neural signaling, and psychosocial stress. Understanding these drivers allows tailored interventions that modulate both peripheral and central pain pathways, moving beyond empirical diets toward individualized, mechanism focused care for pediatric FAPDs.[5]

Emerging Therapeutic Strategies for Pediatric and Adult IBS

Antispasmodics and Smooth Muscle Relaxants

Antispasmodic agents remain the cornerstone of RAP management, directly alleviating smooth muscle hyper-contractility. Drotaverine, a selective PDE-IV inhibitor, enhances intracellular cAMP and reduces calcium influx, producing potent smooth muscle relaxation without anticholinergic effects. Hyoscine, Mebeverine, and Peppermint oil offer comparable relief through distinct mechanisms muscarinic blockade, direct myotropic action, or TRPM8 activation.[6,4] Collectively, these agents interrupt the spasm pain hypersensitivity cycle, providing faster symptomatic improvement and high tolerability, including in pediatric populations (Table 2).

Drotaverine Hydrochloride in Children with Recurrent Abdominal Pain

Drotaverine is an effective and safe pharmaceutical agent in the management of recurrent abdominal pain of childhood. It provides symptomatic relief in children with recurrent abdominal pain. Additionally, Drotaverine was associated with fewer episodes of abdominal pain during its regular use. The precise mechanism by which Drotaverine can relieve abdominal pain is due to its antispasmodic properties, which is devoid of anticholinergic activity.[7]

Efficacy and Safety of Drotaverine Hydrochloride in IBS

Drotaverine, an antispasmodic, has a good relaxing effect on intestinal smooth muscle, which helps in alleviating pain and does not have side effects such as anticholinergics. Result of

Table 2: Mechanism Based Benefits of Common Antispasmodics in RAP and IBS

Drug	Mechanism	Evidence
Drotaverine	PDE IV inhibitor, ↓Ca^{2+} influx	Pediatric RAP, rapid relief, well tolerated
Peppermint oil	TRPM8 activation, smooth muscle relaxation	IBS pain and bloating reduction
Hyoscine	Muscarinic blockade	Symptom reduction in abdominal cramps
Mebeverine	Muscarinic blockade	Effective for GI spasm

a double blind trial showed that the decrease of pain was 47% in the IBS group as compared with 3% in the placebo group.[8]

Neuromodulators

Neuromodulators, including Tricyclic Antidepressants (TCAs), SSRIs, SNRIs, and gabapentinoids, act on central pain pathways, reducing visceral.[3] TCAs slow intestinal transit and raise the pain threshold, useful for IBS-C or IBS-D with predominant pain. SSRIs/SNRIs may also improve comorbid anxiety or depressive symptoms.[6]

Psychological and Behavioral Interventions

Behavioral interventions exploit the gut brain axis to modulate symptom perception, stress response, and illness behaviour. Evidence supports:

- **Cognitive Behavioral Therapy (CBT):** Improves coping strategies, reduces attentional bias towards abdominal pain, and mitigates symptom related anxiety.[2,4]
- **Gut Directed Hypnotherapy:** Reduces pain severity and frequency, comparable to dietary interventions in refractory IBS. [4]
- **Biofeedback:** Targets autonomic dysregulation and abdominal muscle tone, enhancing symptom control. [4]

Access to these therapies may be limited, and sustained benefits often require repeated sessions.

Dietary and Integrative Approaches Beyond Fibre

Dietary interventions complement pharmacotherapy in IBS management:

- **Low FODMAP Diet:** Restricts fermentable carbohydrates, reduces osmotic load and colonic gas production, improving bloating and stool consistency. Clinical studies report 68–86% symptom improvement.[5]
- **Elimination Diets:** Lactose or gluten free regimens may benefit sensitive individuals.[5]
- **Herbal Formulations:** Peppermint, curcumin, and fennel oil provide smooth muscle relaxant and anti-inflammatory effects.[4]
- **Mind Body Therapies:** Yoga, mindfulness, and relaxation techniques reduce stress induced symptom exacerbation.[4]

Integration of dietary and behavioral strategies enhances outcomes beyond single interventions.

Future Directions

Emerging therapies include TRPV1 antagonists, mast cell stabilizers, cannabinoid receptor modulators, and serotonergic pathway targeted drugs. Research on microbiome immune neural interactions may inform precision treatments for pediatric and adult IBS. Multi modal strategies combining pharmacologic, dietary, and behavioral approaches are likely to maximize symptom control and quality of life.[9]

Conclusion

Recurrent abdominal pain represents a chronic, multifactorial disorder rooted in dysregulated gut brain microbiota interactions, visceral spasm, and hypersensitivity, rather than a purely psychosomatic condition. Conventional interventions such as fiber and probiotics offer limited benefit because they do not directly address these underlying mechanisms.

Emerging strategies including smooth muscle relaxants (e.g., Drotaverine), neuromodulators, behavioral therapies, and targeted dietary interventions reflect a paradigm shift toward mechanism based care. Such multi modal approaches, when tailored to the individual's pathophysiological profile, can interrupt the spasm pain hypersensitivity cycle, improve symptom control, and enhance quality of life for children and adults with recurrent abdominal pain.

Future research should focus on biomarker guided personalization of therapy, exploring microbiome, neuro-immune, and sensory signaling pathways to refine this integrative treatment model.

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