

神經與精神用藥評估-2
纖維肌痛與腸躁症的臨床關連
性用藥

Fibromyalgia and Irritable Bowel
Syndrome

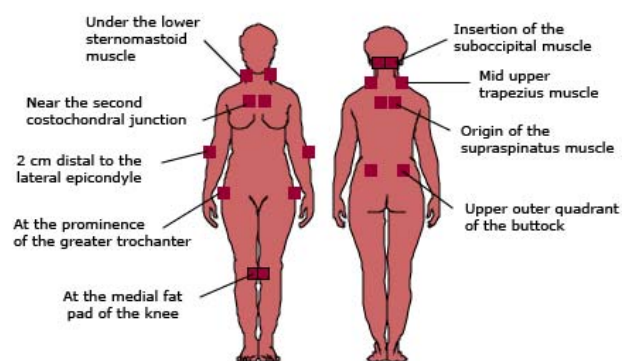
**The IBS-Fibromyalgia
Connection**

- 60% of IBS patients also suffer from fibromyalgia syndrome (FMS).
- 70% of FMS patients have reported experiencing symptoms of IBS.
- Could there be a common cause for both conditions ?
 - Functional disorder
 - Cognitive behavior therapy
 - Certain types of prescription drugs

Chronic Pain Syndromes Comorbidities

- Fibromyalgia
- Irritable Bowel Syndrome
- Depression
- Anxiety

Tender points in fibromyalgia **Fibromyalgia**



The 18 "tender points" important for the diagnosis of fibromyalgia. Note the bilateral symmetry of the labeled regions. Tenderness on palpation of at least 11 of these sites in a patient with at least a three month history of diffuse musculoskeletal pain is recommended as a diagnostic standard for fibromyalgia.

Adapted from: Goldenberg, DL, Hosp Pract (Off Ed) 1989; 24:39.



Diagnostic criteria for the chronic fatigue syndrome

Major criteria

1. New onset of fatigue lasting six months, severe enough to reduce daily activity to less than 50 percent of the patient's premorbid activity level.
2. The exclusion of other conditions that can produce fatigue.

Minor criteria

Symptom criteria

1. Low grade fever: temperature 37.5 to 38.6°C orally or chills
2. Sore throat
3. Painful cervical or axillary lymph nodes
4. Generalized muscle weakness
5. Muscle pain
6. Postexertional fatigue lasting more than 24 hours
7. Generalized headaches
8. Migratory arthralgias
9. Neuropsychological complaints (photophobia, transient visual scotomata, forgetfulness, excessive irritability, confusion, difficulty thinking, inability to concentrate, or depression)
10. Sleep disturbance
11. Acute onset of symptoms over a few hours to a few days

Physical criteria (determined by the physician on two occasions at least two months apart)

1. Low-grade fever
2. Nonexudative pharyngitis
3. Palpable cervical or axillary lymph nodes up to 2 cm in diameter

UpToDate

Fibromyalgia -MEDICATIONS

- Choice of medications - antidepressants
- Low doses and built up slowly
- A low dose of a tricyclic medication at nighttime , especially in the elderly.
- Duloxetine or [milnacipran](#) at breakfast
- [Pregabalin](#) or [Gabapentin](#) at night.
- Low dose of an SNRI in the morning with a low dose of an anticonvulsant in the evening

Dual reuptake inhibitors

- Dual reuptake inhibitors — [Duloxetine](#), [milnacipran](#), and [venlafaxine](#) inhibit both norepinephrine and serotonin reuptake and have been studied in patients with fibromyalgia.
- Take duloxetine or [milnacipran](#) at breakfast

Selective serotonin reuptake inhibitors (SSRIs)

- [Fluoxetine](#)
- [Paroxetine](#)
- [Fluvoxamine](#)
- [Citalopram](#)

Combinations

- Combinations of agents that individually inhibit reuptake of norepinephrine and serotonin or use of single drugs that inhibit reuptake of both neurotransmitters (dual serotonin and norepinephrine reuptake inhibitors or SNRIs) may be more useful
- Addition of an SSRI to a tricyclic or use of an SNRI is a reasonable option for a patient with fibromyalgia and depressed mood.
- The combination of 20 mg of **fluoxetine** in the morning with 25 mg of **amitriptyline** at bedtime was more effective

Cyclobenzaprine

- 10 mg near bedtime and increased as tolerated to the larger doses
- change in pain was not significantly different in active or placebo groups after eight or 12 weeks. Changes in pain and the number of tender points were not significantly different between the groups at any time.

Irritable Bowel Syndrome

- Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by chronic abdominal pain and altered bowel habits in the absence of any organic disorder
- relief of symptoms

Treatment of irritable bowel syndrome

- Dietary modification
 - Lactose
 - Exclusion of gas-producing foods
 - Food allergies
 - Gluten sensitivity
 - Carbohydrate malabsorption
- Psychosocial therapies

IBS- MEDICATIONS

- Antispasmodic agents
- Antidepressants
- Antidiarrheal agents
- Benzodiazepines
- 5-hydroxytryptamine (serotonin) 3 receptor antagonists
- 5-hydroxytryptamine (serotonin) 4 receptor agonists

- Lubiprostone
- Guanylate cyclase agonists
- Antibiotics
- Alternative therapies
 - Herbs
 - Probiotics
 - Acupuncture
 - enzyme supplementation

2009 American College of Gastroenterology (ACG) recommendations for the treatment of irritable bowel syndrome (IBS)

Diet and irritable bowel syndrome
Patients often believe that certain foods exacerbate their IBS symptoms. There is, however, insufficient evidence that food allergy testing or exclusion diets are efficacious in IBS and their routine use outside of a clinical trial is not recommended.

Effectiveness of dietary fiber, bulking agents, and laxatives in the management of irritable bowel syndrome
Psyllium hydrophilic mucilloid (ispaghula husk) is moderately effective and can be given a conditional recommendation. A single study reported improvement with calcium polycarboxylate. Wheat bran or corn bran is no more effective than placebo in the relief of global symptoms of IBS and cannot be recommended for routine use. Polyethylene glycol (PEG) laxative was shown to relieve stool frequency, but not abdominal pain, in the small sequential study in adolescents with IBS-C.

Effectiveness of antispasmodic agents, including peppermint oil, in the management of irritable bowel syndrome
Certain antispasmodics (dicyclanil, omeprazole, pinaverium, and peppermint oil) may provide short-term relief of abdominal pain associated in IBS. Evidence for long-term efficacy is not available. Evidence for safety and tolerability is limited.

Effectiveness of antidiarrheals in the management of irritable bowel syndrome
The antidiarrheal agent loperamide is not more effective than placebo at reducing pain, bloating, or global symptoms of IBS, but it is an effective agent for the treatment of diarrhea, reducing stool frequency, and improving stool consistency. Randomized controlled trials comparing loperamide with other antidiarrheal agents have not been performed. Safety and tolerability data on loperamide are lacking.

Effectiveness of antibiotics in the management of irritable bowel syndrome
A short-term course of a nonabsorbable antibiotic is more effective than placebo for global improvement of IBS and for bloating. There are no data available to support the long-term safety and effectiveness of nonabsorbable antibiotics for the management of IBS symptoms.

Effectiveness of probiotics in the management of irritable bowel syndrome
In single organism studies, lactobacilli do not appear effective for patients with IBS; bifidobacteria and certain combinations of probiotics demonstrate some efficacy.

Effectiveness of the 5-HT₂ receptor antagonists in the management of irritable bowel syndrome
The 5-HT₂ receptor antagonist alosetron is more effective than placebo at relieving global IBS symptoms in male and female IBS patients with diarrhea. Potentially serious side effects including constipation and colon ischemia occur more commonly in patients treated with alosetron compared with placebo. The benefits and harms balance for alosetron is most favorable in women with severe IBS and diarrhea who have not responded to conventional therapies. The quality of evidence for efficacy of 5-HT₂ antagonists in IBS is high.

Effectiveness of 5-HT_{1A} (serotonin) receptor agonists in the management of irritable bowel syndrome
The 5-HT_{1A} receptor agonist tegaserod is more effective than placebo at relieving global IBS symptoms in female IBS-C patients and IBS-M patients. The most common side effect of tegaserod is diarrhea. A small number (0.11 percent) of cardiovascular events (myocardial infarction, unstable angina, or stroke) were reported among patients who had received tegaserod in clinical trials.

Effectiveness of the selective C-2 chloride channel activators in the management of irritable bowel syndrome
Lubiprostone in a dose of 8 micrograms twice daily is more effective than placebo in relieving global IBS symptoms in women with IBS-C.

Effectiveness of antidepressant agents in the management of irritable bowel syndrome
Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are more effective than placebo at relieving global IBS symptoms, and appear to reduce abdominal pain. There are limited data on the safety and tolerability of these agents in patients with IBS.

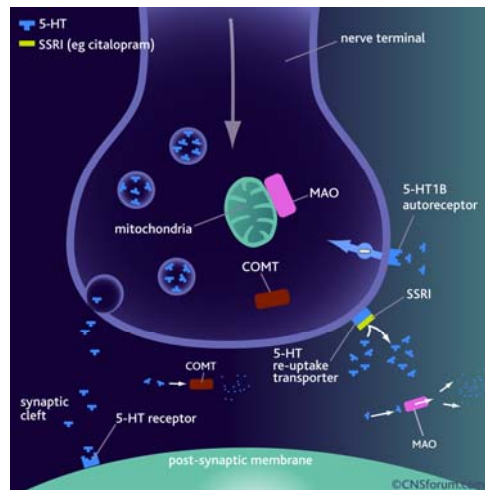
Effectiveness of psychological therapies in the management of irritable bowel syndrome
Psychological therapies, including cognitive therapy, dynamic psychotherapy, and hypnotherapy, but not relaxation therapy, are more effective than usual care in relieving global symptoms of IBS.

Effectiveness of herbal therapies and acupuncture in the management of irritable bowel syndrome
Available randomized controlled trials mostly tested unique Chinese herbal mixtures, and appeared to show a benefit. It is not possible to combine these studies into a meaningful meta-analysis; however, and overall, any benefit of Chinese herbal therapy in IBS continues to potentially be confounded by the variable components used and their purity. Also, there are significant concerns about toxicity, especially liver failure, with use of any Chinese herbal mixture; a systematic review of trials of acupuncture was inconclusive because of heterogeneous outcomes. Further work is needed before any recommendations on acupuncture or herbal therapy can be made.

IBS: irritable bowel syndrome; IBS-C: constipation-predominant irritable bowel syndrome; IBS-M: mixed irritable bowel syndrome; 5-HT₂: 5-hydroxytryptamine (serotonin) 2 receptor agonists; 5-HT_{1A}: 5-hydroxytryptamine (serotonin) 1A receptor agonists.
Data from: American College of Gastroenterology IBS Task Force. An Evidence-Based Position Statement on the Management of Irritable Bowel Syndrome. *Am J Gastroenterol* 2009; 104:31.

神經與精神用藥評估

SSRI Mechanism



來源網址: pharmamotion.com.ar/differenc...of-action

Fluoxetine

- 抑鬱症、暴食症、強迫症
- 20 to a maximum of 80 mg/day
- **Fibromyalgia**
- **Headache**
- **Diabetic neuropathy**
- **Obesity**
- **Tinnitus**
- **Premature ejaculation**
- **Hot sweats**

Paroxetine

- 抑鬱症、強迫症、恐慌症、**Social phobia**、**Posttraumatic stress disorder**
- **20-40mg/day**
- **Fibromyalgia**
- **Headache**
- **Diabetic neuropathy**
- **Obesity**
- **Tinnitus**
- **Premature ejaculation**
- **Hot sweats**
- **Insomnia**

Fluvoxamine

- 重度憂鬱症及強迫症
- **50-300mg/day. hs.**
- Daily dose above 150 mg should be given in 2 doses. max. 300 mg/day.
- **Fibromyalgia**
- **Prostatic pain**

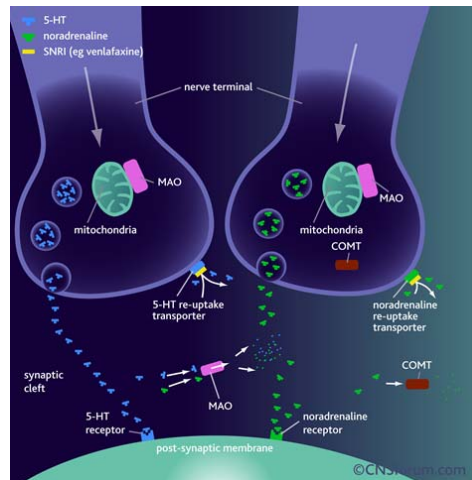
Citalopram

- 鬱症之治療及預防復發、恐慌症
- 20 to 60 mg/day.
- **Fibromyalgia**
- **Headache**
- **Diabetic neuropathy**
- **Obesity**
- **Tinnitus**
- **Premature ejaculation**
- **Hot sweats**

Sertraline

- 鬱症、強迫症、恐慌症、創傷後壓力症候群、社交恐懼症及經前不悅症。
- 50 mg qd.
- increased to 50 mg qd after 1 wk
- max. 200mg /day.
- Alzheimer's disease; Adjunct
- Non-cardiac chest pain
- Clozapine adverse reaction - Obsessive-compulsive disorder
- Flashbacks

SNRI- Mechanism



來源網址: pharmamotion.com.ar/differenc...of-action

Venlafaxine

- 鬱症(泛焦慮症、社交焦慮症)
- GAD: initial, 37.5 mg qd, increased of 75 mg/day at least 4 days. max. 225mg/day.
- Major depressive disorder: 37.5 mg tid. max. 225mg/day(outpatient). 300mg/day(inpatient).
- Panic disorder: 37.5mg/day, increased to 75 mg/day after 1 week.
- **Fibromyalgia**
- **Cancer pain**
- **Diabetic neuropathy**
- **Hot sweats**
- **Tension-type headache; Prophylaxis**

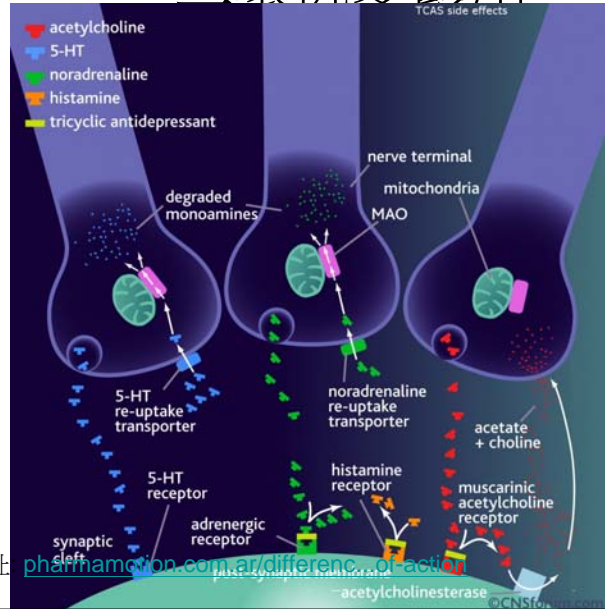
Duloxetine

- 重鬱症
- 20 mg bid. up to 60 mg qd or 30 mg bid.
- Fibromyalgia
- Diabetic peripheral neuropathy - Pain
- Urinary incontinence
- Cancer pain

Atypical antidepressant

- Milnacipran
- 重型憂鬱症
- 50 mg bid.
- Fibromyalgia: initial, 12.5 mg qd; 12.5 mg bid on days 2 and 3; 25 mg bid on days 4 to 7; maintenance, 50 mg bid; max. 100 mg bid

三環抗憂鬱劑



來源網址 pharmaction.com.ar/difference_of_action

Side effects of tricyclic antidepressants

Anticholinergic	Gastrointestinal
Dry mouth	Nausea
Constipation	Vomiting
Urinary retention	Dyspepsia
Blurred vision	Anorexia
Paralytic ileus	Altered taste
Cardiovascular	Neurologic
Tachycardia	Ataxia
Palpitations	Tremors
Arrhythmias	Paresthesias
Hypertension	Mental clouding
Hypotension	Sedation
Heart block	
Myocardial infarction	

Side effects of antidepressant medications*

Drug	Anticholinergic	Drowsiness	Insomnia/agitation	OH [•]	Cardiac arrhythmia	GI distress	Weight gain ^Δ
Tricyclics and tetracyclic							
Amitriptyline	4+	4+	0	4+	3+	0	4+
Amoxapine	1+	2+	2+	2+	2+	0	1+
Clomipramine	3+	3+	4+	3+	2+	3+	3+
Desipramine	1+	1+	1+	2+	2+	0	1+
Doxepin	3+	4+	0	2+	2+	0	3+
Imipramine	3+	3+	1+	4+	3+	1+	3+
Maprotiline	1+	4+	0	2+	1+	0	2+
Nortriptyline	1+	1+	0	1+	2+	0	1+
Protriptyline	2+	1+	1+	2+	2+	0	0
Trimipramine	3+	4+	1+	2+	2+	0	3+
Selective serotonin reuptake inhibitors							
Citalopram	0	0	1+	0	0	3+	0
Escitalopram	0	0	1+	0	0	3+	0
Fluoxetine	0	0	2+	0	0	3+	0
Fluvoxamine	0	1+	1+	0	0	3+	0
Paroxetine	1+	1+	1+	0	0	3+	0
Paroxetine CR	1+	1+	1+	0	0	1+	0
Sertraline	0	0	2+	0	0	3+	0
Dopamine norepinephrine reuptake inhibitors							
Bupropion	0	0	2+	0	1+	1+	0
Bupropion SR	0	0	1+	0	1+	1+	0
Bupropion XL	0	0	1+	0	1+	1+	0
Serotonin norepinephrine reuptake inhibitors							
Duloxetine	0	0	2+	0	0	3+	0
Venlafaxine	0	0	2+	0	0	3+	0
Venlafaxine XR	0	0	2+	0	0	1+	0
Serotonin modulators							
Nefazodone	1+	2+	0	1+	0	2+	0
Trazodone	0	4+	0	1+	1+	1+	1+
Noradrenergic and specific serotonergic antidepressant							
Mirtazapine	1+	4+	0	0	0	0	4+
Monoamine oxidase inhibitors							
Isocarboxid	1+	1+	2+	2+	0	1+	1+
Phenelzine	1+	2+	1+	3+	0	1+	2+
Seligiline	1+	0	1+	1+	0	0	0
Tranylcypromine	1+	1+	2+	2+	0	1+	1+

* Scale: 0 = none, 1+ = slight, 2+ = low, 3+ = moderate, 4+ = high.
[•] OH: orthostatic hypotension.
^Δ Weight gain over 6 kg.
[⊗] Caution: can cause liver failure. Not available in Europe, Canada, and several other countries.

Amitriptyline

- the most widely studied TCA in chronic pain
- 25 to 50 mg, usually given as a single bedtime dose
- dry mouth, constipation, fluid retention, weight gain, grogginess, and difficulty concentrating are common. Such side effects and possible cardiotoxicity limit use in elderly patients.

Desipramine

- Agoraphobia
- Alcoholism - Depression
- Attention deficit hyperactivity disorder
- Bulimia nervosa
- Cocaine withdrawal
- Depression
- Depression, Refractory
- Diabetic neuropathy
- Drug withdrawal, Phencyclidine
- Interstitial cystitis, chronic
- Irritable bowel syndrome
- Obsessive-compulsive disorder; Adjunct
- Panic disorder
- Postherpetic neuralgia
- Posttraumatic stress disorder
- Ventricular arrhythmia

Imipramine

- **Depression**
- **Diabetic neuropathy**
- **Panic disorder**
- **Urinary incontinence**
- **Agoraphobia**
- **Bulimia nervosa**

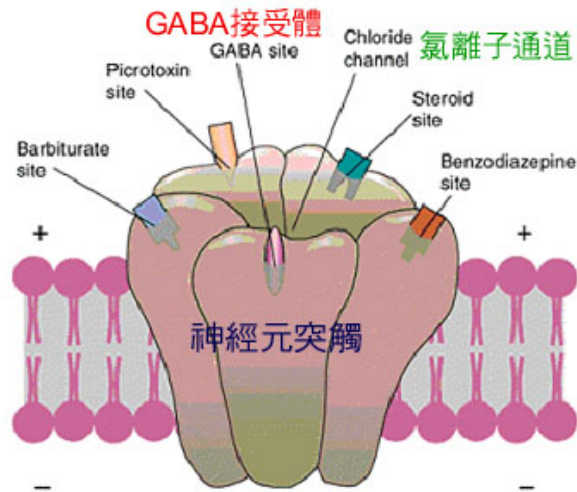
Nortriptyline

- Depression
- Irritable bowel syndrome
- Diabetic neuropathy
- Neurogenic bladder
- Premenstrual dysphoric disorder

ANTICONVULSANTS

- Phenytoin
- Carbamazepine
- Oxcarbazepine
- Valproic acid
- Clonazepam
- the newer agents
 - Gabapentin
 - Pregabalin

Benzodiazepines



Benzodiazepines for chronic pain

Drug	Route of administration	Dose
Diazepam (Valium)	PO/IM/PR	2.5 mg Q 3 to 6 hours
Lorazepam (Ativan)	PO/IV/IM	0.5 to 2 mg Q 3 to 6 hours
Midazolam (Versed)	PO/IV/SC (can be continuous infusion)	1 to 3 mg Q 1 to 3 hours
Clonazepam (Klonopin)	PO	Up to 1.5 mg/day

Muscle relaxants for chronic pain

Drug	Dose
Cyclobenzaprine	10 mg TID (10 to 40 mg/day)
Carisoprodol (Soma)	350 mg TID
Baclofen (Lioresal)	5 mg QD, titrated gradually to 5 to 10 mg TID
Methocarbamol (Robaxin)	1500 mg QID

