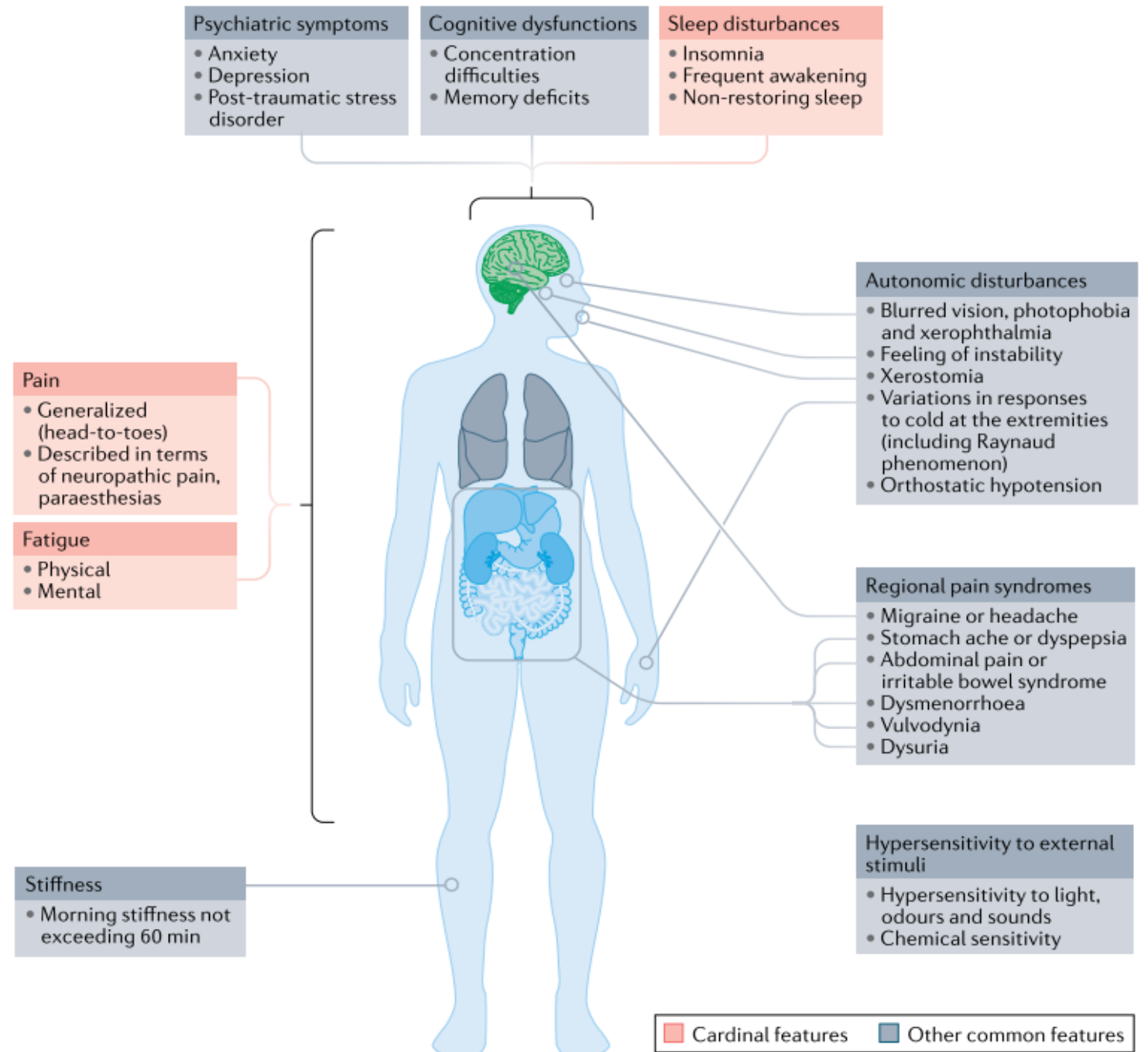


Fibromialgia

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Sarzi-Puttini P, Giorgi V, Marotto D, Atzeni F. Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. Nat Rev Rheumatol. 2020;16(11):645-660. doi:10.1038/s41584-020-00506-w

Criteria

A patient satisfies modified 2016 fibromyalgia criteria if the following 3 conditions are met:

- (1) **Widespread pain index** (WPI) ≥ 7 and **symptom severity scale** (SSS) score ≥ 5 OR WPI of 4–6 and SSS score ≥ 9 .
- (2) **Generalized pain**, defined as pain in at least 4 of 5 regions, must be present. Jaw, chest, and abdominal pain are not included in generalized pain definition.
- (3) Symptoms have been generally present for at least 3 months.
- (4) A diagnosis of fibromyalgia is **valid irrespective of other diagnoses**. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.

Ascertainment

(1) WPI: note the number of areas in which the patient has had pain **over the last week.** In how many areas has the patient had pain? Score will be between 0 and 19

Left upper region (Region 1)

Jaw, left^a

Shoulder girdle, left

Upper arm, left

Lower arm, left

Left lower region (region 3)

Hip (buttock, trochanter), left

Upper leg, left

Lower leg, left

Right upper region (Region 2)

Jaw, right^a

Shoulder girdle, right

Upper arm, right

Lower arm, right

Right lower region (Region 4)

Hip (buttock, trochanter), right

Upper leg, right

Lower leg, right

Axial region (Region 5)

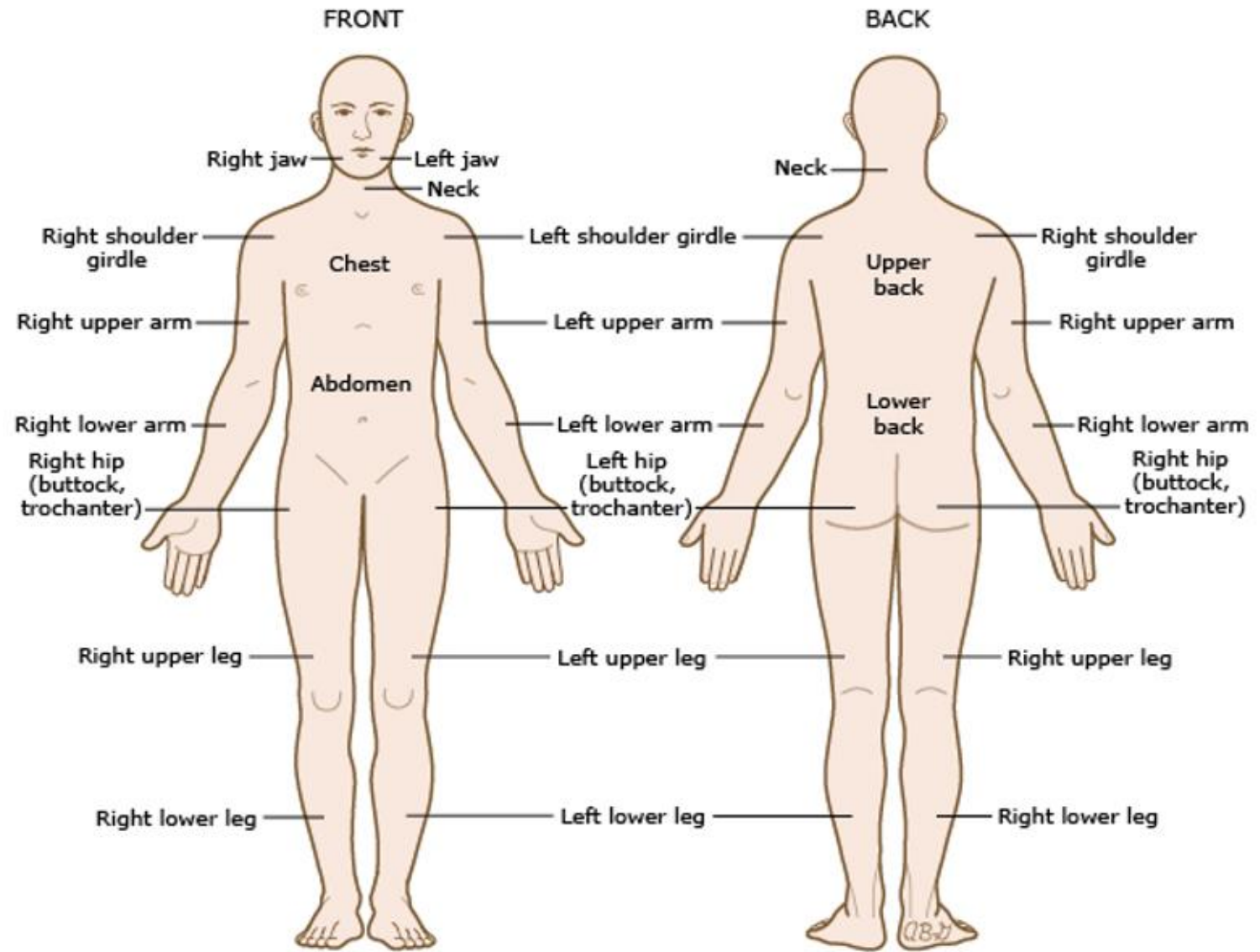
Neck

Upper back

Lower back

Chest^a

Abdomen^a



The total number of the 19 noted anatomic regions in which the patient has had pain over the last week equals the widespread pain index.

(2) Symptom severity scale (SSS) score

Fatigue

Waking unrefreshed

Cognitive symptoms

For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:

0 = No problem

1 = Slight or mild problems, generally mild or intermittent

2 = Moderate, considerable problems, often present and/or at a moderate level

3 = Severe: pervasive, continuous, life-disturbing problems

The symptom severity scale (SSS) score: is the sum of the severity scores of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) (0–9) plus the sum (0–3) of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months:

The symptom severity scale (SSS) score: is the sum of the severity scores of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) (0–9) plus the sum (0–3) of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months:

- (1) Headaches (0–1)**
- (2) Pain or cramps in lower abdomen (0–1)**
- (3) And depression (0–1)**

The final symptom severity score is between 0 and 12

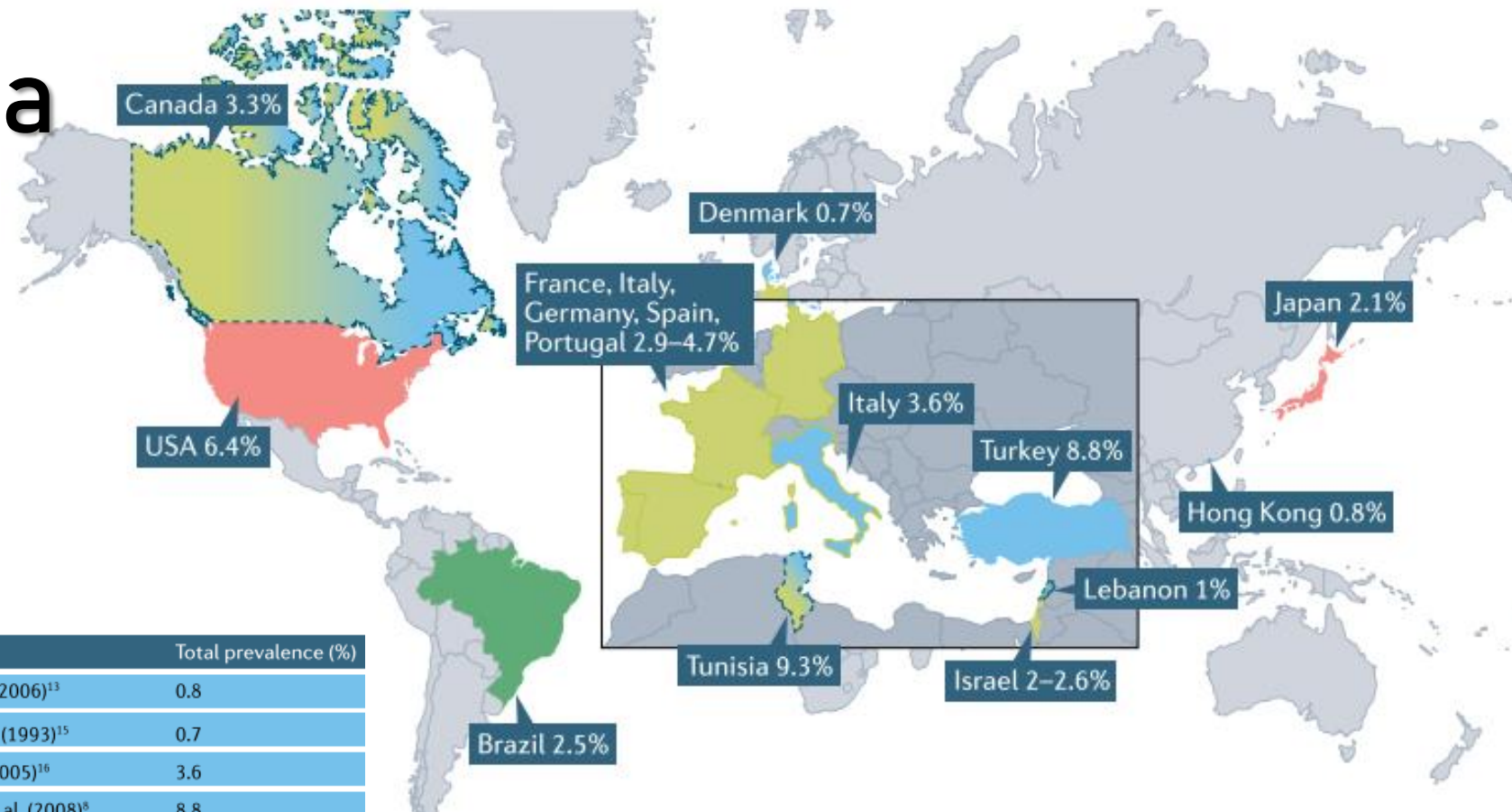
The fibromyalgia severity (FS) scale is the sum of the WPI and SSS

Diagnosi differenziale

Table 2. Differentiating Key Disorders From Fibromyalgia

<i>MEDICAL DISORDER</i>	<i>DIFFERENTIATING SIGNS AND SYMPTOMS</i>
Rheumatologic	
Rheumatoid arthritis	Predominant joint pain, symmetric joint swelling, joint line tenderness, morning stiffness >1 hour
Systemic lupus erythematosus	Multisystem involvement, joint/muscle pain, rash, photosensitivity, fever
Polyarticular osteoarthritis	Joint stiffness, crepitus, multiple painful joints
Polymyalgia rheumatica	Proximal shoulder and hip girdle pain, weakness, stiffness, more common in the elderly
Polymyositis or other myopathies	Symmetric, proximal muscle weakness and pain
Spondyloarthropathy	Localization of spinal pain to specific sites in the neck, mid-thoracic, anterior chest wall, or lumbar regions, objective limitation of spinal mobility due to pain and stiffness
Osteomalacia	Diffuse bone pain, fractures, proximal myopathy with muscle weakness
Neurologic	
Neuropathy	Shooting or burning pain, tingling, numbness, weakness
Multiple sclerosis	Visual changes (unilateral partial or complete loss, double vision), ascending numbness in a leg or bandlike truncal numbness, slurred speech (dysarthria)
Infectious	
Lyme disease	Rash, arthritis or arthralgia, occurs in areas of endemic disease
Hepatitis	Right upper quadrant pain, nausea, decreased appetite
Endocrine	
Hyperparathyroidism	Increased thirst and urination, kidney stones, nausea/vomiting, decreased appetite, thinning bones, constipation
Cushing syndrome	Hypertension, diabetes, hirsutism, moon facies, weight gain
Addison disease	Postural hypotension, nausea, vomiting, skin pigmentation, weight loss
Hypothyroidism	Cold intolerance, mental slowing, constipation, weight gain, hair loss

Epidemiologia



Criteria and/or questionnaire	Country or region	Study	Total prevalence (%)
1990 ACR	Hong Kong	Scudds et al. (2006) ¹³	0.8
	Denmark	Prescott et al. (1993) ¹⁵	0.7
	Italy	Salaffi et al. (2005) ¹⁶	3.6
	Turkey	Turhanoglu et al. (2008) ⁸	8.8
The 2010 ACR criteria	Japan	Nakamura et al. (2014) ⁷	2.1
	USA	Vincent et al. (2013) ¹²	6.4
LFESSQ	Israel	Ablin et al. (2012) ¹⁴	LFESSQ-4: 2.6 LFESSQ-6: 2.0
	France, Italy, Germany, Spain and Portugal	Branco et al. (2009) ⁵	LFESSQ-4: 4.7 LFESSQ-6: 2.9
COPCORD	Brazil	Rodrigues Senna et al. (2004) ¹⁰	2.5
LFESSQ and the 1990 ACR criteria	Canada	White et al. (1999) ¹¹	3.3
	Tunisia*	Guermazi et al. (2008) ⁹	9.3
COPCORD and the 1990 ACR criteria	Lebanon	Chaaya et al. (2011) ⁶	1
	World	Queiroz (2013) ¹	2.7

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Nociplastic pain



Pain that arises from *altered nociception* despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.

Panel 1: Overarching principles for diagnosis of nociplastic pain

- A detailed clinical history that includes:
 - A pain complaint
 - Associated fatigue and sleep disturbance
 - Associated mood and memory problems
 - Other somatic symptoms such as sensitivity to sensory stimuli
 - Other organ system symptoms that are distant from the primary pain complaint
 - Functional status
- Comprehensive physical examination to identify other conditions that could function as a peripheral pain trigger (eg, osteoarthritis or peripheral neuropathy)
- Selective testing that is condition-specific (eg, laboratory tests, imaging, or specific investigations as recommended by relevant guidelines)
- Selective use of symptom-specific questionnaires (eg, sleep, mood, fatigue, or global function)
- Assessment of severity of pain (eg, mild, moderate, or severe)
- Avoid unnecessary investigations or specialist referrals

Panel 2: Clues in patient's history suggestive of nociplastic pain syndrome

- Childhood and adolescent symptoms of pain (eg, headache, abdomen, or low back)
- General symptoms (eg, fatigue and cognitive problems)
- Hypersensitivity to environmental stimuli (eg, light or sound)
- Psychological symptoms (eg, anxiety or depression)
- Symptoms causing a high amount of emotional strain
- A family history of chronic pain and mental health problems
- High use of health-care services (eg, many doctor visits or investigations)
- Poor or no response to conventional analgesics (including opioids)

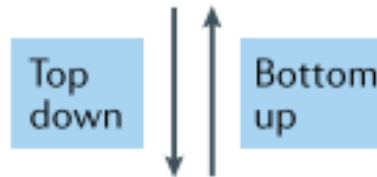
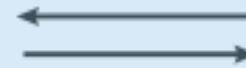
Extrapolated from the EULAR revised recommendations for the management of fibromyalgia.⁴² EULAR=European League Against Rheumatism.

Fisiopatologia

Central nervous system

- Activation of pain areas
- Altered brain connectivity
- ↓ Pain inhibitory signals and paradoxical stimulation
- ↓ Noradrenaline, 5HT, dopamine and opioid receptors
- ↑ Substance P and excitatory neurotransmitters (such as glutamate)

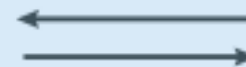
- Low resilience
- Maladaptive stress coping
- Sleep alterations
- Depression and anxiety
- Autonomic alterations
- Genetic factors



Body periphery (sensory neurons, joints, viscera and immune cells)

Peripheral sensitization
(↓ nociceptive threshold)

- Neuroinflammation
- Small fibre neuropathy
- Peripheral nociceptive stimuli or any chronic painful disease
- Genetic factors



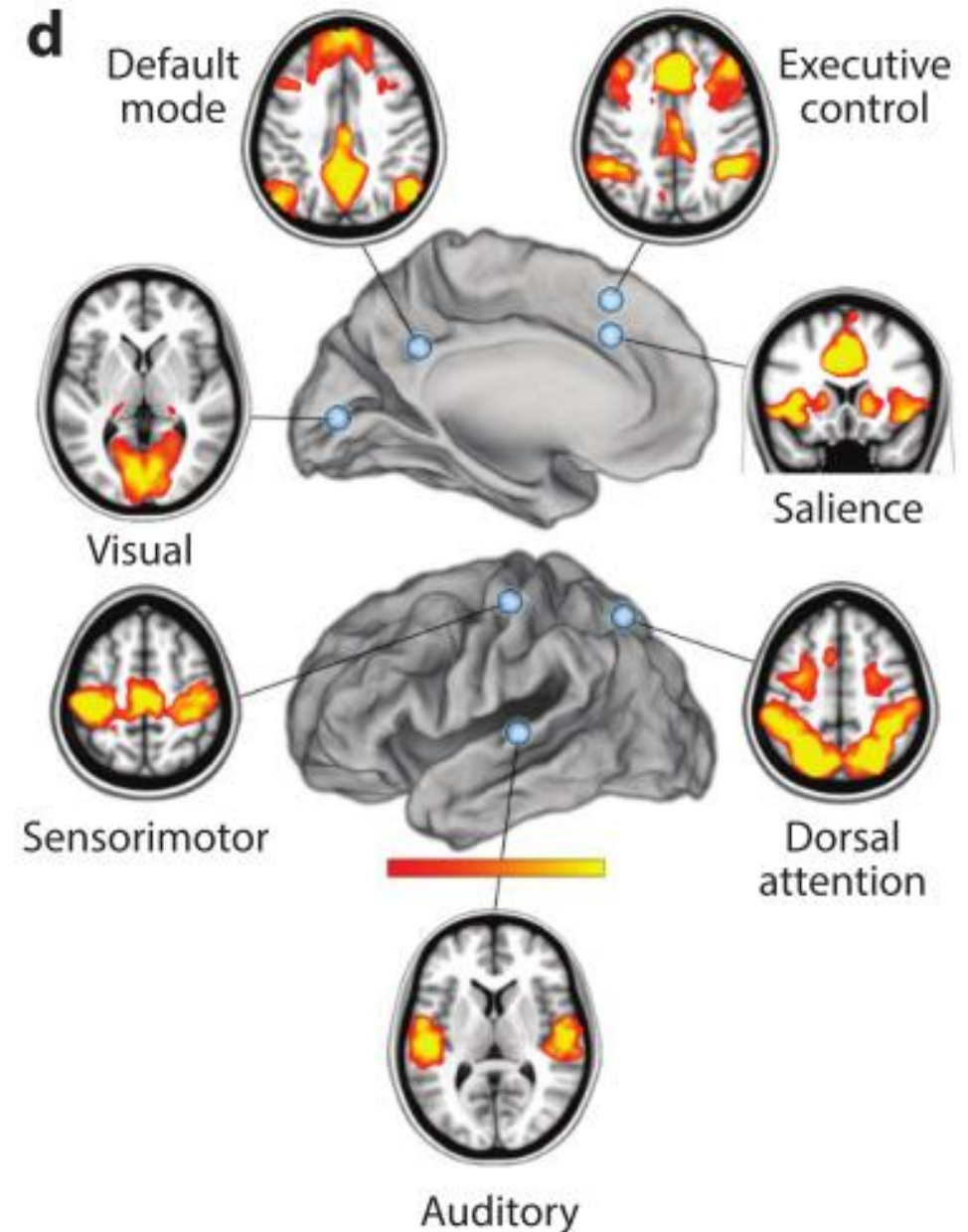
Brain Networks

Salience Network SN

insula anteriore-corteccia cingolata
dorsale anteriore-amigdala-striato
ventrale-substantia nigra

Default Mode Network

corteccia prefrontale ventro-mediale
e dorsomediale- corteccia cingolata
posteriore-precuneo + corteccia
parietale laterale



Default Mode Network ^a

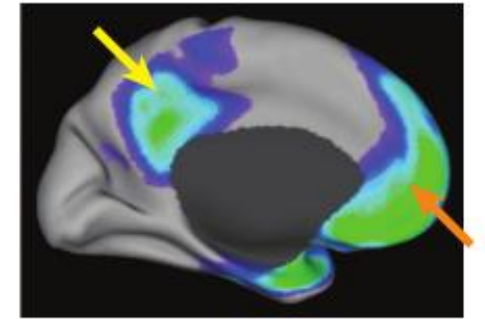
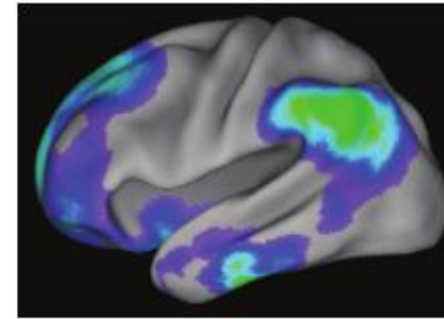
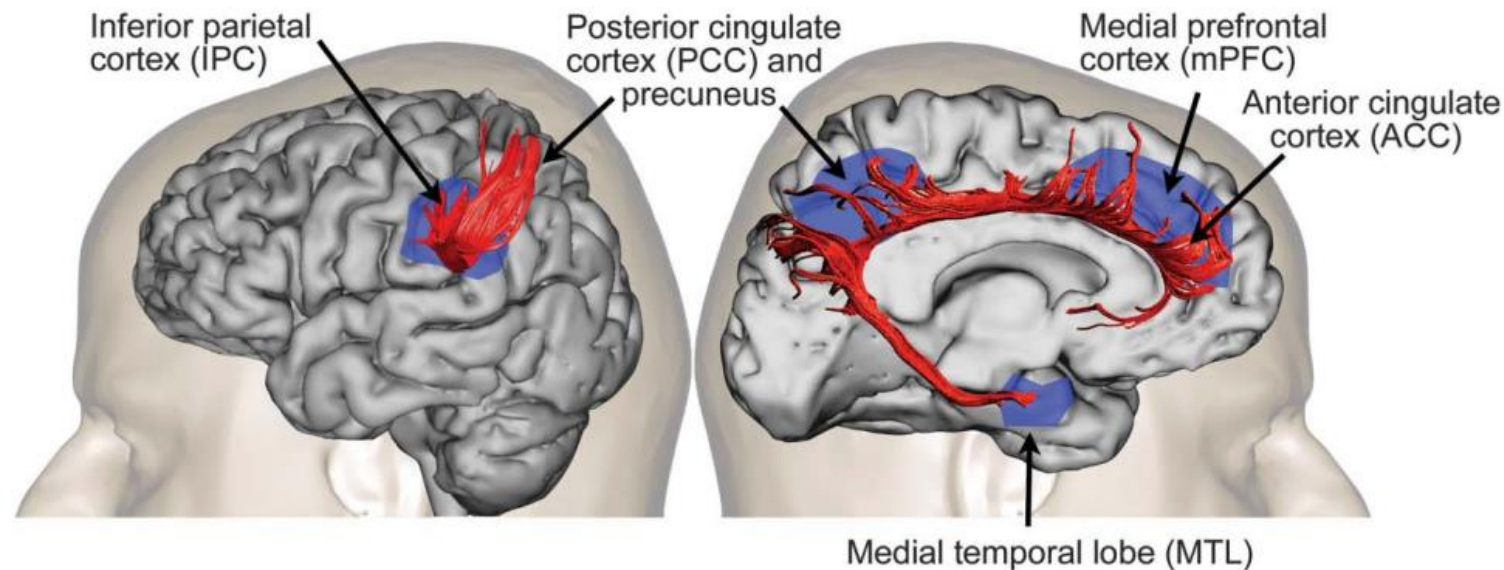


Figure Lateral and medial view of the default-mode network of the left hemisphere



The medial regions of the default-mode network are connected through the cingulum, whereas the inferior parietal cortex is connected to the precuneus and posterior cingulate cortex through a short intraparietal tract. The tracts are reconstructed using diffusion tensor imaging tractography.

Alterazione Brain Networks

- alterazione funzionale lobo temporale mediale (amigdala, ippocampo, giro paraippocampale) → Ipervigilanza agli stimoli sensitivi → After pain sensation
- ↑ connettività di Grigio Periacqueduttale (PAG) con insula, corteccia prefrontale, c. cingolata anteriore → ↓↓ vie discendenti inibitorie
- ↓ connettività di PAG con Salience Network (insula anteriore-c. cingolata dorsale anteriore-amigdala-striato ventrale-substantia nigra) e Default Mode Network (corteccia cingolata posteriore-corteccia prefrontale-circonvoluzione angolare) \propto catastrofismo
- Alterazioni morfometriche aspecifiche di aree corticali, riduzione ippocampo (eccitossicità?)

Neuropatia delle fibre di piccolo calibro

- Sono state dimostrate alterazioni delle piccole fibre a livello dell'arto inferiore prossimale
- Riduzione della densità delle piccole fibre alla biopsia cutanea
- Correlazione con parestesie
- Non chiaro il ruolo patogenetico

Conseguenza di iperattività della trasmissione glutamatergica insulare?

Trigger di aumento compensatorio della elaborazione centrale dello stimolo doloroso?

Espressione di patologia multisistemica immunomediata?