TG		
Pathological changes	Treatment	Treatment effective against
CGRP ↑ PACAP-27 ↓ PACAP-38 ↓ PGE_2 ↑ TRPV1 ↑ 5-HT_7 receptor ↑ cAMP ↑ PKA ↑ $ERK_{1/2}$ ↑ CREB ↑ C-fos ↑ Neuronal sensitization Mitochondrial dysfunction	Ketoprofen	CGRP, PGE_2
	Nimesulide	CGRP, PGE_2
	Etoricoxib	PGE_2
	Flunarazine	CGRP, TRPV1
	Xiongmatang Extract	CGRP, TRPV1
	Electro-acupuncture	5-HT_7 receptor, cAMP, PKA, $ERK_{1/2}$, c-fos, CREB, neuronal sensitization
	TAK-242	c-fos

Supplementary Table S1: Summary of pathological changes in the TG, Changes in the TG following IS, and the effect of experimental treatments and their potential associated targets. For detailed references we refer to the text.

BRAIN/SPINAL CORD		
Pathological changes	Treatment	Treatment effective against
CGRP ↑ 5-HT ↓ GABA ↓ GABABR1/GABABR2 ↓ Glutamate ↑ VEGF ↑ BDNF ↑ nNOS ↑ α7nACh receptor ↓ JNK ↑ CREB ↑ IL-18 ↑ NF-κB ↑ IL-1β ↑ TNF-α ↑ FKN ↑ CX3CR1 ↑ MyD88 ↑ TRIF ↑ IκB ↑ Microglia ↑ Astrocytes ↑ c-Fos ↑ Neuronal sensitization Synaptic plasticity ↓ Changes in functional connectivity Descending inhibitory pathways ↓ BBB permeability ↑↓ White matter volume ↑	Sumatriptan	VEGF
	Baclofen	CGRP, glutamate, PKA, CREB, c-fos, synaptic plasticity
	H89	CGRP, glutamate, CREB, c-fos, synaptic plasticity
	Propranolol	c-fos, neuronal sensitization
	Amitriptyline	Synaptic plasticity
	anti-IL18	IL-18, NF-κB
	PNU-282987	CGRP, α7nACh receptor, JNK, IL-18, TNF-α, microglia, astrocytes
	Electroacupuncture	Neuronal sensitization
	TAK-242	c-fos
	Wuzhuyu decoction	c-fos

Supplementary Table S2: Summary of pathological changes in the Brain/Spinal cord, Changes in the Brain/Spinal cord following IS, and the effect of experimental treatments and their potential associated targets. For detailed references we refer to the text.

TNC		
Pathological changes	Treatment	Treatment effective against
CGRP ↑ Substance P ↑ NO ↑ BDNF ↑ NGF ↑ 5-HT_7 receptor ↓ mGluR5 ↑ $P2X_4$ receptor ↑ $P2Y_{14}$ receptor ↑ ASIC3 ↑ TNF-α ↑ IL-1β ↑ FKN ↑ CX3CR1 ↑ Microglia ↑ C-fos ↑ Neuronal sensitization cAMP↑ PKA ↑ $ERK_{1/2}$ ↑ PKC ↑ p38 ↑ EAAT3 ↑ TrKB ↑ CREB ↑ Synaptic plasticity ↑ EphB2/EphrinB2 ↑ CaMKII ↑ Mitochondrial dysfunction SIRT1 ↓ PGC-1α ↓ mTOR ↑ Autophagy BBB permeability ↑↓	Sumatriptan	CGRP, 5-HT, TNF-α, IL-1β, c-fos
	anti-NGF	CGRP, ASIC3, PKC, c-fos
	Chelerythrin	CGRP, ASIC3, c-fos
	APETx2	CGRP, c-fos
	MPEP	CGRP, Substance P, mTOR, autophagy
	Rapamycin	CGRP, Substance P, IL-1β, autophagy
	Minocycline	IL-1β, TNF-α, microglia
	Electroacupuncture	5-HT_7 receptor, cAMP, PKA, $ERK_{1/2}$, CREB, c-fos
	EphB1-Fc	CGRP, Substance P, synaptic plasticity
	TAK-242	c-fos
	PP2	CGRP, Substance P, synaptic plasticity
	Genistein	CGRP, Substance P, synaptic plasticity
	ANA-12	CGRP, EAAT3, c-fos
	TNP-ATP	CGRP, BDNF, $P2X_4$ receptor, EAAT3, p38, c-fos
	SIRT1720	CGRP, Substance P, SIRT1, PGC-1α, mitochondrial dysfunction
	Wuzhuyu Decoction	CGRP, TNF-α, IL-1β, c-fos

Supplementary Table S3: Summary of pathological changes in the TNC, Changes in the TNC following IS, and the effect of experimental treatments and their potential associated targets. For detailed references we refer to the text.