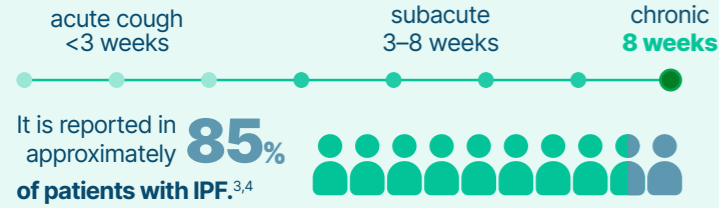


## What is Chronic Cough?

Chronic cough, defined as a cough that lasts **≥8 weeks**, is highly prevalent in **patients with IPF**.<sup>1,2</sup>



The mean number of coughs in patients with IPF is **672-905 coughs/day**.<sup>5,6</sup> Coughs tend to be more frequent and more severe in the daytime than at night.<sup>7,8</sup>

In a prospective, multicentre study of patients with IPF, greater cough severity (VAS ≥30 mm) at baseline was independently associated with **worsening lung function**, greater likelihood of **disease progression**, and **reduced transplant-free survival**.<sup>9</sup>

## Cough effects on patient QOL



Chronic cough **impairs quality of life**, causes **fatigue**, negatively impacts **sleep**, and is **socially isolating**.<sup>4,7,10</sup>

## Cough Hypersensitivity

In cough hypersensitivity, nerve signals become overactive and cause increased cough response **to normal or subthreshold triggers**.

Common triggers include:<sup>3,12-14</sup>



## Sensitisation in Chronic Cough

### Central sensitisation<sup>15-17</sup>

- Mechanisms in the CNS **amplify nerve fibre inputs**
- Normal afferent nerve fibre activity can produce **heightened cough responses**
- Reduced cough suppression** occurs due to loss of inhibitory nerve activity

### Signal transmission<sup>15-17</sup>

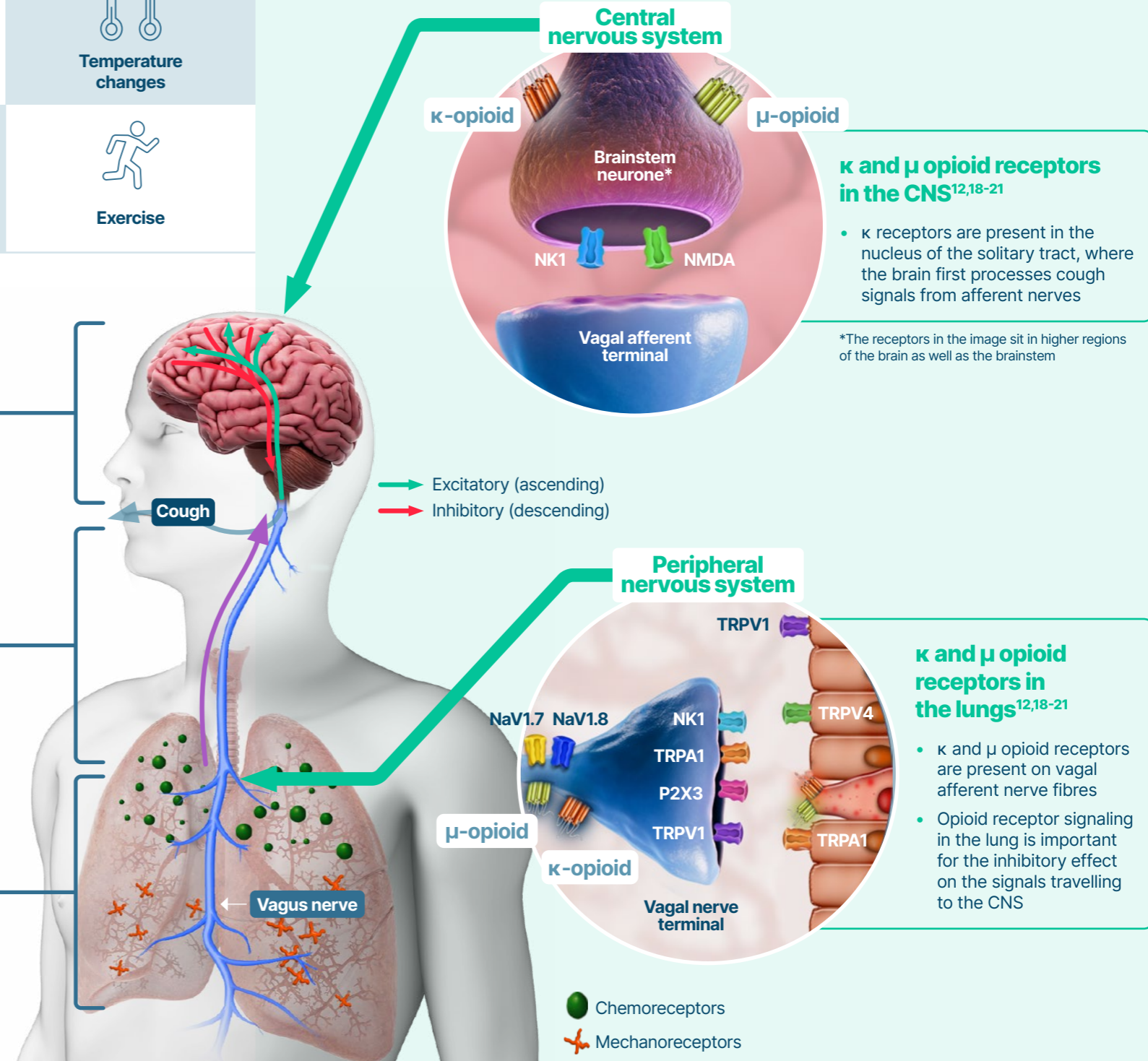
- Amplified nerve signals** are sent to the brain

### Peripheral sensitisation<sup>15-17</sup>

- Afferent nerve fibres** become **more excitable** due to local tissue damage, mechanical stress, and loss of lung tissue
- Triggering stimuli are **more likely** to cause **afferent nerve activation**

## Role of opioid receptors and cough hypersensitivity

Opioid receptor signalling modulates sensitisation by reducing peripheral and central excitatory neurotransmission and enhancing central inhibitory pathways.<sup>15-17</sup>



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## Abbreviations

CNS: central nervous system; IPF: idiopathic pulmonary fibrosis; NaV1.7: sodium voltage-gated channel alpha subunit 9; NaV1.8: sodium voltage-gated channel subtype 1.8; NK1: neurokinin 1 receptor; NMDA: N-methyl-D-aspartate receptor; P2X3: purinergic receptor P2X subtype 3; QoL: Quality of life; TRPA1: transient receptor potential ankyrin 1; TRPV1: transient receptor potential vanilloid 1; TRPV4: transient receptor potential vanilloid 4; VAS: Visual Analog Scale.