Note: Studies of clinical relevance to our findings.

Sleep-disordered breathing can result in intermittent episodes of hypoxia, the cumulative effect of which includes the possible loss of brain gray matter, impaired cognitive function, and increased mortality. Here, preBötC neuronal loss caused multiple repeated episodes of (apnea-induced) hypoxia that would likely have caused further neuronal loss. We suggest that this effect was minor during the early stages of sleep-disordered breathing, because the disturbances were limited in total duration, so the initial changes in breathing pattern were the direct effect of NK1R preBötC neuron loss. Beyond this point, however, the cumulative effect of intermittent hypoxia resulting from prolonged apneas could have induced neuronal death, not necessarily restricted to the preBötC, further disrupting respiratory pattern during sleep and wakefulness.

Adults with syringobulbia (with brainstem symptoms or MRI evidence of medullary syrinx) breathe relatively normally during wakefulness but during sleep, breathing patterns are severely disrupted by the occurrence of central apneas or severe hypopneas. Respiratory disorders in sleep are common in patients with some neurodegenerative diseases e.g., amyotrophic lateral sclerosis (ALS), multiple systems atrophy (MSA), or Parkinson’s disease (PD), while breathing during wakefulness is considered otherwise normal. Many of these patients die suddenly during sleep. Additionally, patients with MSA or PD also have impaired chemosensitivity to hypoxia, which in rats can result from loss of preBötC neurons.