



Expectation and dyspnoea: the neurobiological basis of respiratory placebo effects

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A neural dyspnoea placebo effect was found; expectations of dyspnoea increase the central neural processing of dyspnoea and respiratory effort as seen by activation of the periaqueductal gray and deactivation of the rostral anterior cingulate cortex <http://bit.ly/3p2TsA6>

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Abstract

Cues such as odours that do not *per se* evoke bronchoconstriction can become triggers of asthma exacerbations. Despite its clinical significance, the neural basis of this respiratory placebo effect is unknown.

We investigated this effect in a functional magnetic resonance imaging (fMRI) study involving 36 healthy volunteers. The experiment consisted of an experience phase in which volunteers experienced dyspnoea while being exposed to an odorous gas ("Histarinol"). Volunteers were told that Histarinol induces dyspnoea by bronchoconstriction. This was compared with another odorous gas which did not evoke dyspnoea. Dyspnoea was actually induced by a concealed, resistive load inserted into the breathing system. In a second, expectation phase, Histarinol and the control gas were both followed by an identical, very mild load. Respiration parameters were continuously recorded and participants rated dyspnoea intensity after each trial.

Dyspnoea ratings were significantly higher in Histarinol compared with control conditions, both in the experience and in the expectation phase, despite identical physical resistance in the expectation phase. Insula fMRI signal matched the actual load, *i.e.* a significant difference between Histarinol and control in the experience phase, but no difference in the expectation phase. The periaqueductal gray showed a significantly higher fMRI signal during the expectation of dyspnoea. Finally, Histarinol-related deactivations during the expectation phase in the rostral anterior cingulate cortex mirrored similar responses for placebo effects in pain.

These findings highlight the neural basis of expectation effects associated with dyspnoea, which has important consequences for our understanding of the perception of respiratory symptoms.