The Neurobiological Basis of the Placebo Effect and Potential Therapeutic Applications

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Two patients, Patient A and B, are diagnosed with the same chronic pain condition after a catastrophic car accident. Both patients experience the same type of chronic pain around their neck and lower back. Both patients receive the same prescription from the same doctor, except one bottle of pills does not contain any active drug. Both patients experience pain relief from their symptoms in a few weeks and improve their condition drastically with the treatment. How is this possible if only one of the patients received an active drug compound? The placebo (pla-see-boh) effect, or placebo response, can be described as the “improvement of symptoms” in an individual after receiving a substance under a certain context that is supposed to have no real therapeutic effect (Ortega et al., 2022). But what does this really mean? Is there a neurobiological basis to the placebo effect? Is there an opportunity for the usage of placebo treatments in a clinical setting? In the United States, a country largely influenced by big pharmaceutical companies, delving deeper into the biological basis and further therapeutic application might be seen as a potential threat but nevertheless, a necessary effort to make.

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Let’s delve a little deeper into how a placebo effect works in the big complex blob that is the human brain. One of the most important factors for a placebo to work is context and setting (Cai and He, 2019). For example, it’s more likely for someone to trust the words of a confident doctor in a white coat than your average joe in a sketchy alley. When you're in the appropriate setting, neurons in your dorsolateral prefrontal cortex begin to fire (Ortega et al., 2022). This area of the brain, located right behind your forehead, is basically like the quality check controller of the brain. If the dorsolateral prefrontal cortex finds good quality information, that likely means it’s important! So this information gets sent off to other areas in the brain, specifically the areas responsible for releasing dopamine and self made opioids (Bennedetti et al., 2005).

The brain can, in fact, produce its own natural opioids called endogenous opioids, and they provide the same level of pain relief as exogenous opioids! From here the brain is releasing feel good chemicals and the placebo effect is in full speed. It can cause even greater changes in the immune system and hormone system (Ortega et al., 2022)

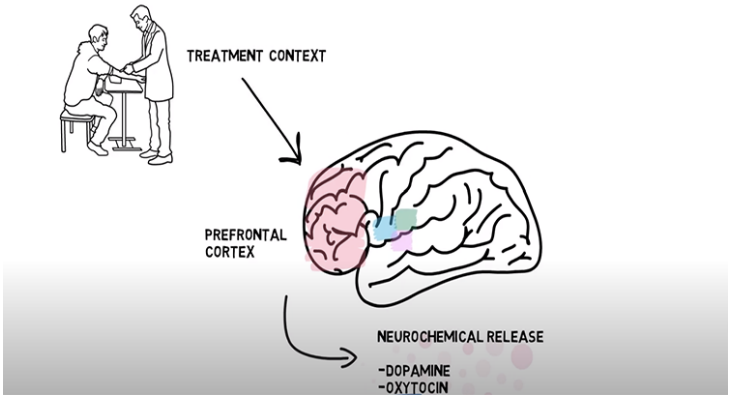

Figure 1. The context in which a placebo treatment is administered is crucial for the corresponding signals to activate the pathways starting from the prefrontal cortex (BrainFacts/SfN).

But if all it takes is to activate that prefrontal cortex, why don’t all placebo treatments work? Well, that answer is a bit more complex but has a lot to do with the context the placebo is received in and the internal beliefs of the person receiving the placebo. Belief also has a major influence on the placebo effect being successful. In fact, the main area of the brain that stores mental representations of the world in order to create our own internal beliefs is the prefrontal cortex (Sathyanarayana Rao et al., 2009). The prefrontal cortex is the area that starts to bring meaning to the signals and stimuli around us, something with meaning can be stored as an internal belief. A “stronger” belief can be correlated to more neurons firing in the prefrontal cortex, and when activated in the right setting, can produce the benefits of the placebo. The more we practice the same connection over and over, the stronger its effects (Sathyanarayana Rao et al., 2009). Similarly, if the belief is negative, and those connections are strengthened, then there won’t be a perceived change overall (“This doesn’t work!”). So, in reality, we really do become what we think.

References

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