

## **The observation that does (not) hurt. Observational learning of placebo hypoalgesia and nocebo hyperalgesia induced by operant conditioning**

Placebo is mostly known as a sugar pill, that is often used in research on drug effectivity. It is something that works, although it seems it shouldn't, and evokes what is known as the placebo effect. What is less known, the placebo can also cause an opposite effect and induce negative health outcomes (such as nausea). Placebo may also be an effective pain reliever (or, unfortunately, pain enhancer). So far, several methods of inducing pain alleviation (hypoalgesia) and pain deterioration (hyperalgesia) by administering a placebo have been discovered and most of them rely on learning mechanisms. The first is learning through prior experience, i.e., creating an association between an active agent (e.g., a painkiller to relieve pain) and its appearance (e.g., red colour), which results in pain relief after administration of a pill (this time a placebo) of the same colour. Another type of learning (so-called operant conditioning) has also been successfully used to evoke pain relief after using a placebo. It consists of learning by consequences: giving a reward (e.g., money) after administration of a placebo (e.g., in a form of a cream) each time when a person experiences less pain and giving a punishment (e.g., taking away money) for feeling more pain.

What is more, as people are social beings, also observing other people experiencing pain relief after administration of a placebo may cause a pain alleviation in the observer (as well as it can cause deterioration of pain after observing the same effect in observed person). This type of observation is just another form of learning (so-called vicarious) and uses principles of classical and/or operant conditioning mentioned before. Up to date research on observing other people experiencing less or more pain after placebo administration was limited to observation of other people rating pain in a specific manner, so purely through creating associations via another person (so using classical conditioning). The other type of learning, operant, has not been studied in that regard. Thus, we decided to fill in this research gap for two reasons. Firstly, as we know from everyday life, observing other people receiving rewards and punishments influences our own behaviour, as it can be a hint on how to behave ourselves in order to optimize our functioning in the society (as we all want to receive rewards and avoid punishment), and observing consequences of pain behaviours are not different in this regard. Sometimes we may for example observe that, after an accident our relative receives a lot of attention when he or she is in pain, we also know that they do not have to go to work and still receive a pension. This observation may potentially influence our behaviour in a similar situation in the future and e.g., prolong or intensify our pain and can significantly contribute to our wellbeing. Secondly, operant type of learning is considered to be a mechanism of transforming acute pain (lasting shortly) to chronic pain (long-lasting pain) and observing it in others may potentially influence an individual's pain experience in a similar way, which may be important in clinical practice.

Thus, the project presented here aims to compare the effect of observation of pain behaviours in others after placebo administration, using the classical conditioning and operant conditioning procedures, as well as verify the influence of expectancy and some of individual characteristics (empathy, sensitivity to being rewarded and punished) on these effects. To achieve this, two experiments are planned. Participants will be healthy volunteers that will receive painful electrocutaneous stimulation and they will undergo a procedure of either classical conditioning or operant conditioning themselves or will observe one of those learning procedures in a model. The first study will verify if pain alleviation (hypoalgesia) can be caused by observation of operant conditioning in others after placebo administration and compare it with the same effect caused by observation of classical conditioning. The second experiment will examine and compare the same influence but in pain deterioration (hyperalgesia) after placebo distribution. We will also measure physiological indicators of pain (galvanic skin response, heart rate) during the experiment. The results of this project may be important not only for subsequent experimental studies on operant conditioning as a mechanism of placebo hypoalgesia and hyperalgesia, but above all for clinical practice. Rewards and punishers occurring and observed in everyday life (including in a doctor's office) may affect the effectiveness of pain treatment. The results of planned research may help to make a use of this mechanism to be the basis for the design of effective pain therapies by specialists.