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Review

The negative Hawthorne effect: Explaining pain overexpression

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ABSTRACT

In medicine, the positive Hawthorne effect is defined as decreased symptom expression due to being observed. This effect occurs in addition to the decrease in symptom experience due to the placebo effect. Symptom overexpression, in contrast, whether related to conscious or to unconscious factors, defines the negative Hawthorne effect, which should be distinguished from the nocebo effect, defined as an increase in symptom experience. For instance, the negative Hawthorne effect can result in patients who seem fully relaxed evaluating their pain intensity at 11 on a 10-point Scale. The negative Hawthorne effect stems from multiple factors including a wish to receive greater consideration or priority management status; concern about failing to meet criteria for receiving a new treatment or being included in a therapeutic trial; conformism related to cultural factors or to circumstance (e.g., avoiding the canceling of a surgical procedure in the event of a last-minute improvement); disease mongering; a desire to be taken seriously by family and friends; a quest for secondary benefits; use of the evaluation to express frustration about being ill or bitterness at receiving a lower level of support; a gap between the expectation of complete relief and the true effectiveness of treatments; and pain exacerbation, with loss of reliability of pain intensity measurements, due to anxiety, guilt, depression, nervosity, catastrophizing, kinesiophobia, or repeated evaluations using methods that involve negative suggestions such as considering the worst pain imaginable. A sequence of a strong negative Hawthorne effect before treatment prescription followed by a strong positive Hawthorne effect after treatment initiation may make a greater contribution than the placebo effect to the improvements produced by treatments for pain.

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The Hawthorne effect is defined as a change in the results of an experiment due to the subjects being aware that they are observed. Greater motivation and/or a wish to meet the expectations of the observers are the usual results of the Hawthorne effect [1,2].

In medicine, the Hawthorne effect is often conflated with the placebo effect [3], although the two involve different mechanisms. The placebo effect is defined as an improvement that a patient actually experiences when a sham treatment induces the release of neuromediators that suppress the symptom (e.g., endorphins) or make it less unpleasant (e.g., dopamine) [4]. In contrast, the positive Hawthorne effect is defined as a decrease in symptom expression that is dependent on the circumstances or observer. For instance, a hospitalized patient may indicate a pain intensity score of 4/10 if the observer is a friendly medical student after having given a score of 6/10 a few minutes earlier when the observer was a stern resident. When the variable under study is subjective, the Hawthorne effect can be very marked and stronger than the placebo effect sensu stricto.

Hawthorne effects can explain why changes attributed to the placebo effect – but chiefly due to Hawthorne effects – can last several months. An example is persistent pain relief after sham vertebroplasty, without cement injection. In double-blind randomized studies, women in the sham vertebroplasty group reported a nearly immediate decrease in pain intensity from 6 to 3 followed by persistence of this degree of pain relief for 3 months, whereas controls who had neither the verum nor the sham procedure reported a pain intensity of 5 after 3 months [5]. The release of endorphins or dopamine responsible for placebo effects cannot last 3 months.

Most studies of Hawthorne effects focused on improvements. The possibility that the Hawthorne effect may result in symptom exacerbation has not yet been considered. Nevertheless, awareness by the patients that they are being observed and evaluated may increase the expression of various symptoms. The frequent incrimination of nocebo effects in this exacerbation [6,7] may be inappropriate in some cases. Broadly speaking, nocebo effects are responsible for an actual increase in pain intensity, due to the release of neuromediators such as cholecystokinin (which also

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Box 1

The true mean pain Score decline induced by various analgesics compared to a placebo, assessed using a 10-point visual analog Scale, has been determined in several meta-analyses. Here, these declines are compared to the pain score increase induced by negative suggestions that generated negative Hawthorne-placebo effects.

Oral acetaminophen: −0.84 (95% CI: −0.73 to −0.95) [42]
Step II opioids: −1.06 (95% CI: −0.76 to −1.35) [42]
Step II opioids: −1.20 (95% CI: −0.6 to −1.8) [42]
Negative suggestions: +0.74 (95% CI: +0.4 to +1.08) [13]

antagonizes placebo effects) [8,9]. Similarly, nocebo effects sensu stricto are defined as the induction of adverse effects that are actually perceived when the patient receives a negative suggestion.

Negative Hawthorne effects have been quantified by comparing the response to intravenous treatments given with versus without knowledge by the patient [10]. Patients in both groups were administered the same treatment, considered to be effective (e.g., morphine), using a remote-controlled power syringe. The times at which the injections started and stopped were concealed in one group (hidden-group) and disclosed in the other (open-group). Patients in the open-group reported pain relief as soon as they were told that an injection had started, whereas the time to pain relief was longer in the hidden-group. This difference indicates a nearly instantaneous positive Hawthorne effect in the open-group. In addition, a very rapid increase in pain intensity occurred when the open-group patients learned that the injection had stopped but was not seen in the hidden-group patients [10]. This rebound effect was ascribed to an anti-placebo effect due to the patient's expectation that the treatment effects would be lost immediately at discontinuation of the injection. However, the nearly immediate pain score increase after the end of the injection is far more likely to reflect a negative Hawthorne effect than an anti-placebo effect, although a functional MRI study would be needed to confirm this possibility [11]. The immediate loss of pain relief in the open-group conflicts with the known pharmacological effects of morphine, which persist for 1 to 3 hours after the end of the injection. Furthermore, such a strong anti-placebo effect is not consistent with evidence that the psychological profile of patients who experience marked placebo effects often differs substantially from that of patients prone to nocebo effects. A report [12] that a simple negative suggestion resulted in a mean pain score increase on a 10-point Scale of 0.74, i.e., very close to the smallest clinically significant change of 1.0 [13] (Box 1), supports this hypothesis. Finally, additional support for the existence of negative Hawthorne effects comes from reports of patients who appear perfectly relaxed yet indicate a pain intensity score of 11 on a 10-point Scale.

The objective of this work is to list the main reasons and circumstances that can lead patients to consciously or unconsciously magnify their symptoms. This objective is worthwhile because in many situations, including the management of pain, the sum of Hawthorne effects (secondarily positive but initially negative) can be greater than the true effectiveness of some treatments [14].

1. Conformism as a source of negative Hawthorne effects

The positive Hawthorne effect results in the subject trying to satisfy the observer's expectation of a good outcome. In the seminal experiment [1], manufacturing employees at Hawthorne Works demonstrated increased productivity during an inspection intended to determine whether improved lighting would benefit productivity. The observers noticed that the increase in productivity persisted after the end of the observation period, when the lighting was brought down to its previous level unbeknownst to the workers.

In some circumstances, however, the observers may expect a negative effect, such as the emergence of a new sign that may help to establish a difficult diagnosis. Some patients, particularly those with hypochondria, may magnify a symptom suggested by the physician, thereby leading to a constructed diagnosis. Patients may be particularly prone to this negative effect if they have previously learned via Internet searches [15] that the suggested symptom can be produced by the disease they fear (or hope) they may have. A finicky interview style – as illustrated in the famous play *Knock* by Jules Romain – may contribute to convince a patient with this type of personality that he or she suffers from the disease in question. Disease mongering is a similar phenomenon in which either trivial signs are combined to create the impression that a disease exists or symptom thresholds for disease are lowered to establish a diagnosis or decide on a treatment (Knock strategies).

Conformism can also produce negative Hawthorne effects when a patient is scheduled for surgery to treat a painful condition. The patient may then experience nearly complete pain relief shortly before the time of surgery yet not disclose this change out of respect for the difficulty the surgeon had in scheduling the procedure. If interviewed, the patient may overestimate the intensity of the pain to avoid forcing the surgical team to cancel the procedure at the last minute. In this situation, the pain scores reported to surgeons may be higher than those reported to nurses [16].

Other factors that may influence the scoring and expression of pain include culture [17] and genetic background [18].

2. Pushing for faster management as a reason for negative Hawthorne effects

Pain overexpression due to more or less conscious mechanisms may occur when competition for access to care leads patients to fear they will not be considered as priorities. For instance, understaffing in emergency departments or extended-stay facilities prompt patient to exaggerate the expression of their pain. This mechanism may operate also in pain control centers, which often have long waiting times.

3. A desire to meet activity criteria as a source for negative Hawthorne effects

In everyday practice, gaining access to certain new medications is theoretically dependent on meeting criteria for a minimum level of disease activity. For instance, TNFα antagonist therapy for spondyloarthritis is indicated only if the BASDAI is above 4/10 [19]. Patients who are aware of these activity criteria may exaggerate their reports of pain to gain access to the drug.

Publicity for a new therapeutic method may lead patients to believe that switching from their current treatment to the new treatment would improve their outcomes. They may then spuriously exaggerate their symptoms to convince their physician to give them the treatment they want, which may be a surgical procedure [20].

During clinical trials, the screening visits and collection of informed consent may take time, during which the symptoms may improve to a level that no longer meets inclusion criteria. Patients may then report scores on verbal or analog scales that are above their true level of pain, in order to meet inclusion criteria. Thus, patients, who may or may not have been told of the cutoffs by the physician, may temporarily exaggerate their complaints in order to be randomized and to potentially gain access to the study treatment. This behavior may then cease at the time of the first study drug dose, so that the first post-randomization evaluation may

seem to indicate a very rapid improvement. Studies also indicate that a positive response to recruitment in a trial may result in initial improvements [2,21].

4. Concern about not being taken seriously as a source of negative Hawthorne effects

Patients may exaggerate the expression of their pain if they fear that their healthcare providers, co-workers, and/or family may underestimate their suffering. A trivial example is the dramatic behavior of soccer players injured on the field, which is designed to increase the referee's evaluation of the severity of the foul. Such behavior is not seen in rugby matches, during which the often-rougher physical contact is not punished in the same way.

5. A quest for secondary benefits as a source of negative Hawthorne effects

Patients may exaggerate their complaints to obtain compensation for a work-related injury or to perpetuate a situation they feel is advantageous to them, for instance if they are seeking financial reparation or disability status, a sick leave extension, or the granting of social benefits that depend on being scored above a severity cut-off. This type of negative Hawthorne effect is known as malingering, which is intermediate between simulation and accident neurosis [22].

6. Frustration with the evaluator as a source of negative Hawthorne effects

Patients who are frustrated about not achieving the expected level of relief may exaggerate their complaints to emphasize the inadequacy of their management, even when they have received the best care possible. This behavior may be encouraged by the satisfaction questionnaires handed to patients at discharge, which may lead patients to behave as litigious consumers or to adopt a passive-aggressive behavior. Similar effects may be produced by polemical statements likening healthcare professionals to "brutes in white coats" (the title of a book by M Winckler).

Paradoxically, even when the healthcare worker-patient relationship is very good, for instance during a clinical trial, patients may unconsciously express their bitterness at receiving less attention after the end of the trial by giving higher pain scores than during the trial [23]. A study involving the 8-month follow-up of patients after the end of a trial showed a nearly 50% decline in HAQ scores and 23% to 44% increases in pain and overall patient evaluation scores [23]. However, these changes may reflect antagonism of a positive Hawthorne effect rather than a negative Hawthorne effect.

7. Interference between the evaluation and various emotions as a source of negative Hawthorne effects

Various emotions may increase the level of pain expression. Anxiety is among them. Patients may fear an increase in pain intensity and a worsening of pain-related limitations that would make them unable to carry out their everyday activities. In this situation, adding an anxiolytic agent may be at least as effective as an analgesic and may also prevent analgesic misuse [24]. Reassurance by the healthcare providers should remain the best means of avoiding anxiety-induced exacerbations in pain expression. An early evaluation of patient misconceptions about the severity of their problems may minimize pain expression both by eliminating the negative Hawthorne effect and by inducing a true placebo effect via the conversion of negative auto-suggestion to an expectation by the patient that the future will bring improvements [25].

This healing effect of input from healthcare workers is blunted, however, when depression or neuroticism contributes to worsen the pain [26] or when patients are concerned about a dip in performance that may lead to their losing their job. To assist in interpreting pain scores in everyday practice and in guiding initial treatment decisions, particularly at hospital admission, it would therefore be useful, if allowed by the circumstances, to simultaneously assess psychological factors by completing the Hospital Anxiety and Depression Scale (HADS) [27]. The HADS is easier to use than instruments measuring neuroticism, such as the Big Five Inventory [26]. Questions about the patient's job situation are also useful.

Another emotion associated with the level of pain expression is guilt about experiencing pain that indirectly places a burden on family and friends (e.g., by requiring additional work or causing fatigue among family members acting as carers or by requiring that family vacations be cancelled) [28]. Patients who believe they have failed to do everything in their power to decrease the pain are particularly prone to guilt. This vulnerability has been exploited by advertisements for analgesics ("stop suffering"), which were also designed to encourage physicians to prescribe analgesics.

Another major source of negative Hawthorne effects may be collective frustration generated by politicians and/or the media who fly in the face of the medical evidence by promising that complete pain relief is a realistic goal. Although the advertisements used by pharmaceutical companies are often more circumspect, they sometimes convey subliminal messages that are frustrating or even guilt-producing, such as a photograph, for an osteoarthritis drug, of a 70-year-old woman doing the splits with a broad smile.

Catastrophizing can also produce negative Hawthorne effects. The three dimensions of catastrophizing are rumination, a feeling of helplessness, and symptom magnification [29]. This last dimension is nearly synonymous with a negative Hawthorne effect, and the other two dimensions can act as predisposing factors.

Finally, kinesiophobia [30] may induce a negative Hawthorne effect in some patients, although this point remains to be proven. The worsening of the symptoms serves as a pretext to avoid physical exertion. Improvements that occur after physiotherapy may be partly ascribable in some cases to the correction of such a negative Hawthorne effect.

8. Repeated evaluations as a source of negative Hawthorne effects

Despite the use and misuse of analgesics induced by campaigns to promote pain control, first in the US then elsewhere, the mean pain intensity in the treated population does not seem diminished. Thus, three-quarters of patients using opioids reported persistent severe pain [31]. This finding is further confirmation that analgesics are less effective than believed by the general public and a substantial proportion of healthcare professionals. This misguided optimism can be ascribed in part to inadequate evidence-based evaluations by health authorities of the true efficacy and harmfulness of analgesics. However, the persistence of self-reported severe pain despite opioid therapy may also reflect a tendency of patients to overrate their pain, due to multiple factors.

One explanation may be the high degree of material comfort provided by modern life, which many induce similar behaviors in some patients. Another possible explanation may be algophobia due to three decades of vigorous marketing campaigns targeted at physicians, health authorities, and the general public to eliminate the opiophobia of the past by hyperbolizing pain, thereby inducing opiophilia. Finally, a third explanation may lie in repeated pain eval-

uations, which first became standard practice in the US, then spread to other countries. Admitted patients are asked several times a day to rate their pain intensity using a visual analog scale. The description on the scale of maximum pain as "the worst pain imaginable" may result in negative suggestion. Just as the instruction "Don't think of an elephant" immediately brings forth the image of an elephant, the term "worst pain imaginable" may exacerbate concern that the current pain may increase to unbearable levels. In addition, the term "worst pain imaginable" may contribute to inhibit the development of a placebo effect (which is attenuated or even abolished by anxiety) and to induce a negative Hawthorne effect. Support for this possibility can be found in one of the fundamental rules of mind-body treatment methods (e.g., sophrology, self-hypnosis, and meditation) consisting in eliminating pain from the field of consciousness [32] or in limiting the cognitive and emotional impact of pain. Some admonitions illustrate the risk of self-pity inducing greater vulnerability (with the royal counter-example of Queen Victoria telling her son, the future Edouard VII, to "never explain, never complain"). Many patients with joint disease elect not to complain, as a basic coping mechanism, in contrast to the rumination that characterizes catastrophizing [33].

To assess the potential effects of repeated pain evaluation, randomized double-blind trials in patients with specific disease types and severities could compare changes over time in mean self-assessed pain scores computed from scores obtained several times a day or only at the beginning and end of treatment. The working hypothesis would be that multiple daily assessments increase the consumption of analgesics. However, an important issue is whether the quality of pain relief is better with multiple daily assessments than with less frequent assessments. Thus, without falling into the extreme of accusing the thermometer of causing the fever (here, the pain scoring of causing the pain), the consequences of closely spaced pain assessments deserve investigation [34]. Repeated assessments may induce psychological sensitization, which would then add its effects to the central nervous system sensitization seen in some patients [35]. Focusing unduly on assessments may have benefited pharmaceutical companies rather than patients and physicians, even without considering the hundreds of thousands of deaths caused by opioid misuse in the US [36,37].

The induction of negative Hawthorne effects by excessively frequent pain assessments may constitute a limitation to home self-evaluation by patients with inflammatory joint disease. Tools used for home self-evaluation include the RAPID3 score computed as the sum of a pain Score on a 0–10 visual analog scale and of the functional HAQ Score. Thus, although the RAPID3 Score is rapid and simple to determine and can be used in all musculoskeletal diseases, its use may have limitations [38].

9. Conclusion

The possibility that negative Hawthorne effects can be induced indicates that:

- patient evaluation is not a neutral act, as repeated evaluations may alter the results;
- suggestion can affect not only the experience of symptoms (placebo effect), but also their expression (positive Hawthorne effect, which should be called into play [39], and negative Hawthorne effects, which should be countered); and;
- negative Hawthorne effects may impair coping [33].

Some of the improvements documented during clinical trials are ascribable to the combination of initially negative Hawthorne effects (symptom magnification at inclusion) followed by positive Hawthorne effects (symptom minimization once treatment is started), which produces a difference that is often greater than expected [40]. Thus, a recent randomized double-blind trial in emergency rooms in New York city hospitals compared acetaminophen plus ibuprofen to acetaminophen plus oxycodone. The pain score decrease 2 hours after the dose was similar in the two arms (8.9 to 4.3 and 8.7 to 4.4, respectively, i.e., an improvement of 4.5 points on a 10-point Scale) [41]. Nevertheless, metaanalyses of randomized trials concluded that the true improvement provided by Step III opioids versus the placebo was only 1.2 on a 10-point Scale (i.e., 0.36 more than with oral acetaminophen (Box 1) [42]). Furthermore, in a randomized trial no difference was found between intravenous morphine and intravenous acetaminophen used to treat pain in the emergency room [43]. Over three-quarters of the pain score decline (3.3/4.5 points) in this trial was therefore probably due to a combination of marked negative Hawthorne effects upon arrival in the emergency room (with anxiety and fear of not being treated as a priority resulting in pain overrating at nearly 9/10) followed by placebo and positive Hawthorne effects.

The pharmaceutical industry may reap benefits from the sequence of a negative Hawthorne effect before treatment followed by a positive Hawthorne effect after treatment initiation, as it overestimates the efficacy of their products. Nevertheless, the overrating of pain intensity before treatment is not in the interest of the patients or their physicians. On the opposite, it amplifies pain expression, worsens catastrophizing [44] (which can largely cancel out improvements induced by true therapeutic advances) [29], and may result in analgesic misuse [43].

When conducting clinical trials in patients with inflammatory joint disease, disease intensity and pain intensity must be measured, including by the use of *retrospective* questionnaires designed to capture past pain flares [45]. However, encouraging a high frequency of pain self-assessment may have deleterious effects. For admitted patients, asking whether their pain relief is adequate may be wiser than calling to mind the "worst pain imaginable" several times a day, and making optimistic verbal suggestions may counteract negative Hawthorne effects [46].

Disclosure of interest

The authors declare that they have no competing interest.

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