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Beliefs about medication predict the misattribution of a common symptom as a medication side effect — Evidence from an analogue online study

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ABSTRACT

Objective: Some perceived medication side effects may be 'normal' symptoms that patients misattribute to the medication. Using an analogue approach, we tested if medication beliefs predict whether participants misattribute a headache as a side effect and subsequently intend to stop medication.
Methods: We recruited 690 participants, 223 reporting a past asthma diagnosis. They received information about asthma and Molair, a fictitious asthma treatment modeled on a licensed treatment (montelukast). We varied the description of efficacy and side effects (which did not include headache). Pre-exposure to this information, participants completed the Beliefs about Medicine Questionnaire (BMQ)-General and the Perceived Sensitivity to Medicines Scale (PSM), post-exposure they completed the BMQ-Specific. Participants were asked to imagine they experienced a headache while taking Molair. Finally, they rated whether the headache was a side effect (misattribution) and if they would stop taking Molair (behavioral intention).
Results: Nearly a quarter (170) of participants misattributed the headache to Molair and 69 (10%) subsequently intended to stop Molair. Both outcomes were predicted by general and specific medication beliefs. Odds of misattribution (m) and behavioral intention (i) increased with higher General Harm (ORm = 1.90, ORi = 2.72), General Overuse (ORm = 1.74, ORi = 1.56) and Molair Concern beliefs (ORm = 1.52, ORi = 1.78, all $p < .01$), but decreased with General Benefit (ORm = 0.72, ORi = 0.53) and Molair Necessity beliefs (ORm = 0.72, ORi = 0.70, all $p < .05$).
Conclusion: Symptom misattribution and subsequent intentions to stop Molair were predicted by pre-exposure beliefs about medicines in general and post-exposure beliefs about Molair. Patients with negative medication beliefs may be prone to misattribute symptoms and subsequently stop medication.

Introduction

The prescription of a medicine is one of the most common interventions in affluent healthcare systems. Appropriate medication use is crucial to the management of most long-term conditions that account for the majority of health spending [1]. But, the capacity of medication to improve health is compromised by adverse effects and nonadherence [2,3]. People who experience (and sometimes merely anticipate) side effects are prone to nonadherence [4,5], and consequently less likely to experience the full benefit from their treatment, with implications for morbidity, mortality and healthcare utilization. For patients who take their medication, side effects add to the burden of disease and treatment [6], increase anxiety and reduce quality of life [7,8]. Problems linked to medication side effects in ambulatory (e.g. treatment changes, additional doctor visits) and non-ambulatory settings (e.g. longer hospitalization) were estimated at over $170 billion per year in the US alone [9].

Understanding determinants of side effects therefore has implications for patients and healthcare systems. Side effects are often caused by specific pharmacological effects of medication. For example, aspirin inhibits prostaglandin pathways in the stomach, which can lead to gastric erosion [10]. Psychological factors such as expectations and conditioning [11] also contribute to side effects. Around 20–25% of chemotherapy patients experience nausea or vomiting *before* drug administration [12,13], indicating the importance of non-pharmacological factors in side effect experiences.

The misattribution of symptoms arising due to disease, everyday activities or normal bodily variations, as side effects may be another psychological process contributing to side effect reports [14,15]. Symptoms like dizziness, headache and fatigue are frequently reported as "side effects" by patients receiving placebo in randomized controlled trials [16–19] and are common in healthy individuals not taking medication [20–22].

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In this paper we test whether cognitive representations of specific medications and pharmaceuticals in general [23–26] influence the attribution of symptoms as side effects. Specific medication beliefs are the salient beliefs influencing engagement with a specific treatment for a given condition. They are operationalized in the Necessity Concerns Framework [27,28] which posits that evaluations of prescribed medicines are influenced by judgment of personal necessity for treatment relative to concerns about potential harm [29]. These evaluations are influenced by general 'social representations' of pharmaceuticals as a class of treatment (e.g. whether pharmaceuticals are fundamentally harmful, addictive chemicals that are over-prescribed by doctors [23,26,30]), representations of the health threat (e.g. illness representations) and somatic experiences and attributions (e.g. whether a symptom is attributed to illness or medication) [25,31,32]. Symptom experiences and attributions are therefore a key determinant of how we think about and act upon illnesses [33–35]. Medication beliefs have been linked to side effect reports in prospective clinical samples with rheumatoid arthritis [36], depression [37], and HIV/AIDS [38]. A tendency for individuals with negative beliefs about medicine to attribute everyday 'normal' symptoms to their medication could contribute to these associations.

In this study, we asked participants to imagine taking a fictitious asthma medication and then experiencing a headache (not listed as a side effect of the medication). We probed whether participants attributed the headache as a side effect and subsequently intended to stop the medication. Although this was an analogue study, we wanted to make the scenario presented as concrete and believable to participants as possible. We therefore chose a common disease, asthma [39], so that we could recruit participants online who either had asthma or were familiar with it. Likewise, we chose headache, a common 'everyday' symptom and side effect [22,40,41] to probe symptom attribution. In addition, the experience of side effects, sometimes resulting in the discontinuation of medication, as well as headache "side effects" to placebo have all been documented in studies involving patients with asthma [42,43]. Our primary hypothesis was that participants with negative medication beliefs would be more likely to: [1] Misattribute the headache symptom as a side effect and [2] subsequently intend to stop the medication.

We systematically varied information about the fictitious medication, presenting it as highly or moderately effective and having either frequent or rare side effects. We expected the variation of the patient information to influence people's specific beliefs about the medication (e.g. increased concerns for participants randomized to high side effect frequency information). We also wanted to check whether any effect of beliefs on misattribution and intention were robust across this information variation. We explored whether the hypothesized relationships were similar for participants with and without self-reported previous asthma diagnosis and persisted when controlling for negative affect as a potential confounder. Because we were measuring beliefs about a fictitious medication, we also checked that the associations between general and specific beliefs were consistent with theoretical predictions [24] and previously reported associations [30].

Method

Data was collected in three consecutive waves. Within each wave, participants were randomized to different descriptions of the efficacy and safety of the fictitious medication. In all waves participants completed validated measures of medication beliefs and the symptom attribution vignette. Affect was assessed in wave three.

Participants and recruitment

We included individuals over 18, with and without self-reported past asthma diagnosis. Only one response was allowed per participant (across the three waves). Participants were recruited on online job boards (e.g. Amazon MTurk, Crowd Guru, DailySurveyPanel) where subscribers complete surveys for small monetary rewards (around $0.30 in this study), and an online research website (Psychological Research on the Net). This sampling approach has demonstrated reliability in studies of decision-making, personality and health [44–46].

Materials

Asthma and Molair information

Participants read information about asthma (see Appendix A) structured according to Leventhal's Common Sense Model of illness representations [47,48]. It described asthma causes (airway inflammation and sensitization), triggers (e.g. exercise, pollen), likely consequences, and asthma management (e.g. medicines and lifestyle changes) and asthma symptoms (e.g. difficulty breathing, wheezing) and their episodic nature.

Participants were randomized to one of four written patient information leaflets (PILs) of the fictitious asthma drug Molair (see Appendix B), modeled on the existing asthma medication, montelukast [49]:

1) The "High Efficacy PIL" stated that Molair is highly effective '86.6% of patients reported a *strong improvement* in daytime asthma symptoms' and contained no information about the frequency of side effects.
2) The "Moderate Efficacy PIL" stated that Molair is less effective, '53.2% of patients reported a *small improvement*' and contained no information about the frequency of side effects.
3) The "Low Side Effect Frequency PIL" contained general efficacy information "Molair can be effective in preventing asthma symptoms." and stated that side effects were rare "*in less than 1 in 100 people*".
4) The "High Side Effect Frequency PIL" contained general efficacy information "Molair can be effective in preventing asthma symptoms." and stated that side effects were frequent "*in more than 45 out of 100 people*".

All four PILs contained the same list of 8 side effects, presented in randomized order. Headache was not listed as one of Molair's side effects.

The information was in line with published montelukast efficacy data [50–52] and reported side effect rates to montelukast relative to placebo [53] (low frequency) and placebo in randomized controlled trials [54–56] (high frequency).

Measures

Symptom misattribution and behavioral intention measures

Participants read the following scenario: "*Imagine you are suffering from asthma. You have been taking one 4 mg tablet of Molair every day for the last two weeks. At the beginning of the third week you get a headache*.' They were then asked two questions:

1) Symptom misattribution:

What do you think is the most probable reason for this?" Participants had a choice between five different options (side effect of Molair, onset of a cold, eyestrain, stress, no particular reason). Symptom misattribution was defined as indicating "side effect of Molair" as most likely reason for the headache symptom.

2) Behavioral intention to stop treatment:

Participants indicated which action(s) they would take following the start of the headache (stop taking Molair, speak to a doctor or pharmacist, take over the counter painkiller, rest, other, none of the above). Participants could select as many options as they wished and could specify additional actions. Behavioral intention was operationalized as selecting "stop taking Molair".