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The being a patient effect: negative expectations based on group labeling and corresponding treatment affect patient performance

Katharina A. Schwarz[a,b], Roland Pfister[b] and Christian Büchel[a]

[a]Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
[b]Department of Psychology, University of Würzburg, Würzburg, Germany

ABSTRACT

Patient studies provide insights into mechanisms underlying diseases and thus represent a cornerstone of clinical research. In this study, we report evidence that differences between patients and controls might partly be based on expectations generated by the patients' knowledge of being invited and treated as a patient: the *Being a Patient* effect (BP effect). This finding extends previous neuropsychological reports on diagnosis threat. Participants with mild allergies were addressed either as patients or control subjects in a clinical study. We measured the impact of this group labeling and corresponding instructions on pain perception and cognitive performance. Our results provide evidence that the BP effect can indeed affect physiological and cognitive measures in clinical settings. Importantly, these effects can lead to systematic overestimation of genuine disease effects and should be taken into account when disease effects are investigated. Finally, we propose strategies to avoid or minimize this critical confound.

Introduction

Empirical evidence from controlled patient studies is vital for ensuring progress in modern medicine and psychotherapy. By comparing a patient group with a well-matched healthy control group, the experimenter attempts to pinpoint the disease's effects on a variety of measures to arrive at a detailed clinical picture.

However, psychological findings on the impact of expectations on perception and cognitive function (Schwarz, Pfister, & Büchel, 2016) suggest that the difference between patients and healthy controls is not only determined by the effect of the disease, but also by psychological components that are determined by social role, i.e. the knowledge of being a patient. Patients suffering from a variety of diseases will be expected to perform worse on tasks targeting different functions or to feel more pain than healthy controls (Ferguson, Mittenberg, Barone, & Schneider, 1999). In fact, patients with mild head injuries seem to perform worse in neuropsychological tests when such negative expectations are pointed

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CONTACT Katharina A. Schwarz ✉ katharina.schwarz@uni-wuerzburg.de

out to them before testing ('diagnosis threat', Suhr & Gunstad, 2002). Diagnosis threat has been studied almost exclusively for patients with head or brain injury (Kit, Mateer, Tuokko, & Spencer-Rodgers, 2014; Suhr & Gunstad, 2002, 2005), and these populations might be especially sensitive to expectancy effects due to the clear relation of their diagnosis and the employed neuropsychological measures. Whether similar effects would occur also for patient groups without such links between diagnosis and measures remains to be explored.

Moreover, expectancy effects have been repeatedly reported for pain perception (Büchel, Geuter, Sprenger, & Eippert, 2014; Colloca & Benedetti, 2005; Schwarz et al., 2016; Tracey, 2010) and cognitive functions (Bandura, 1997; Pajares, 1996; Schmader, Johns, & Forbes, 2008; Schwarz et al., 2016; Steele & Aronson, 1995). Negative expectations based on group membership, i.e. being a patient, may thus cause actual increases in pain sensitivity or decreased performance in cognitive tasks. This phenomenon – the 'being a patient' effect (*BP effect*) – could possibly lead to a systematic overestimation of actual disease effects (Figure 1(A)).

To test this hypothesis, we invited participants with mild seasonal allergic rhinitis – a diagnosis that does not imply major impairments – and tested whether negative expectancy effects could still be induced in this sample. We randomly divided them into a 'patient' and a 'control' group following previous studies on patients with head or brain injury (Kit et al., 2014; Suhr & Gunstad, 2002, 2005).

Method

Participants

We recruited participants with mild seasonal allergic rhinitis (*N* = 48), randomly assigned to the *patient* group (*n* = 27; 7 male) and the *control* group (*n* = 21; 6 male). The groups did not differ in age or allergy symptom severity (Table 1). None of the participants was currently under medication. Participants were excluded if there were technical errors during any of the sessions, if they guessed the purpose of the study, if they did not understand the task instructions or if they did not believe the instructions (see osf.io/86m4c for details). All participants gave informed consent. The study was approved by the Ethics Committee of the Medical Council of Hamburg.

Experimental procedure

Participants were tested on two days (Figure 1(B)). On the first day, they were asked to perform an arithmetic task (Beilock, Rydell, & McConnell, 2007; Krendl, Richeson, Kelley, & Heatherton, 2008), a mental rotation task (Peters & Battista, 2008; Shepard & Metzler, 1971), and a Stroop color-word interference task (MacLeod, 1991), to cover relevant independent domains of cognitive functioning. All tasks were computer-administered reaction time (RT) tests with manual responses and task order was randomized across participants. Before each test, participants rated how well they expected to perform during the respective task.

The critical experimental manipulation was performed about one week later. Participants in the *patient* group were told that they would take part in a study on the effects of allergies on pain perception and higher cognitive functions including information why allergies might have negative effects on these cognitive processes.
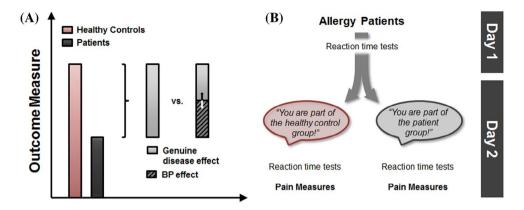
Figure 1. Study rationale and experimental design. **A.** Visualization of how expectancy-related effects of being a patient (BP effect) might inflate typical comparisons of patients with healthy controls. Any performance decrement in patients relative to controls could either result from a genuine disease effect or from a combination of a disease effect and a BP effect of unknown size, thereby leading to a systematic overestimation of the actual disease effect. **B.** Overview of the study design. *Patient* and *control* group only differed in terms of group labeling and initial instruction, not in actual symptom severity.

Table 1. Descriptive data of both groups (2 participants who guessed the true purpose of the study were excluded from these data).

	Patients	Controls
Age (years)	25.19 (.61)	26.05 (.84)
Symptom severity	16.25 (1.03)	15.30 (.84)
STAI T	38.69 (1.47)	38.55 (2.04)
BDI II	5.97 (.91)	6.20 (1.08)
LPS 3	9.77 (1.07)	9.35 (1.21)
LPS 4	8.77 (.95)	8.50 (.84)

Notes: Scores indicate group means, accompanied by standard errors of the mean (SE_M) in parentheses.
Abbreviations: STAI T = State-Trait Anxiety Inventory Trait; BDI II = Beck Depression Inventory II; LPS 3/4 = tests 3 and 4 in the German 'Leistungsprüfsystem' (intelligence test).

Participants in the *control* group were invited as healthy controls in a study on the effects of schizophrenia on pain perception and higher cognitive functions. The experimenter wore a white lab coat in all cases and participants performed the same tasks as on day 1. Afterward, we measured the critical heat pain thresholds. Both groups were interviewed about their allergy symptoms, the *patients* before and the *controls* after the experimental procedure. In the *patient* group, the interview was followed by a short questionnaire to assess whether participants believed the instructions about the allergies' negative effects. More details regarding the employed tasks, sample size calculations and exclusion criteria for all analyses can be found on osf.io/86m4c.

Results

Figure 2 summarizes our central results. Although the *patient* and the *control* group merely differed in group labeling and initial instructions, *patients* showed a lower pain threshold
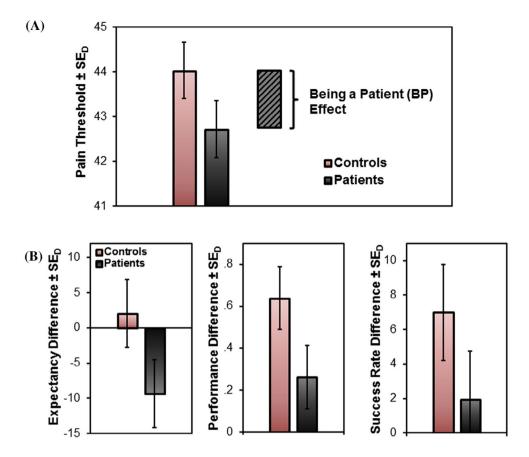
Figure 2. Differences between the patient and control group signify the Being a Patient (BP) effect. **A.** Difference in the pain threshold temperature (°C) between the patient and control group. Error-bars indicate standard errors of the between-group difference (SE$_D$, Pfister & Janczyk, 2013). **B.** (Left) Performance expectancy difference (day 2–day 1). The patient group expected to perform worse after being treated as patients on the second day, whereas the control group's rating pattern remained unchanged. (Center) Performance difference in easy arithmetic equations (day 2–day 1). Patients performed worse on the second day compared with the controls. To facilitate interpretation, performance is displayed as (1/RT [ms])*10^4, i.e. higher scores indicate faster responses on the second day compared to the first day. (Right) Success rate difference (%) in easy arithmetic equations (day 2–day 1). The success rate difference showed a similar trend as the performance scores, indicating that the slower answering pattern in the patient group cannot be explained by speed-accuracy trade-offs. Error bars indicate standard errors of the between-group difference (SE$_D$, Pfister & Janczyk, 2013).

than *controls* (Figure 2(A)), $t(38) = 2.07$, $p = .023$, $d = .65$ (one-tailed due to the directional hypothesis).

BP effects were also present in the cognitive tasks. *Patients* but not *controls* expected to perform worse in the arithmetic task on the second day, $t(41) = 2.36$, $p = .012$, $d = .72$ (*t*-test on the difference scores *day 2–day 1*, Figure 2(B)). This differential effect on the expectancy ratings was mirrored in decreased performance for easy arithmetic equations, $t(41) = 2.38$, $p = .011$, $d = .73$ (Figure 2(B); see osf.io/86m4c for details). Mental rotation performance was not affected differentially (*F*s < 1), whereas a significant difference occurred for accuracy data of the Stroop task, $t(42) = 2.24$, $p = .015$, $d = .68$ (though partly driven by ceiling effects and therefore not further discussed).

Discussion

Our results demonstrate that differences between patients and healthy controls can at least partly be accounted for by the BP effect. We found differences between two groups of patients with mild allergy that differed only in group labeling and initial instructions, not in symptom severity. While stereotype-related effects on patients are beginning to be realized in clinical settings (Cole, Michailidou, Jerome, & Sumnall, 2006; Kit, Tuokko, & Mateer, 2008), the present data indicate that expectancy-based differences might also affect the very process of investigating particular diseases.

Although a clear BP effect emerged in our results, it was not equally present in all measures. Most susceptible to the expectancy manipulation were the pain threshold measure and the arithmetic task, a test heavily relying on working memory (Beilock et al., 2007). This finding replicates previous reports on diagnosis threat for mild traumatic brain injury (Blaine, Sullivan, & Edmed, 2013). Mental rotation (measuring spatial cognition), by contrast, did not elicit the BP effect. This pattern not only shows that BP effects can be obtained for subjective and objective measures alike (Schwarz & Büchel, 2015), but it also gives first indications which domains may be especially prone to yield BP effects in clinical research (cf. Ozen & Fernandes, 2011).

An alternative mechanism that might mediate the observed BP effects may also be a relative improvement of the 'healthy controls' (i.e. a placebo effect based on the emphasis of being healthy) rather than an impairment in the patient group (i.e. a nocebo effect based on the social role of being a patient). This mechanism seems unlikely, however, given previous evidence that placebo effects are harder to elicit than nocebo effects and are often elusive when no conditioning procedures are employed to promote potential placebo effects (Colloca, Sigaudo, & Benedetti, 2008; Schwarz et al., 2016). In any case, the difference between conditions could still be attributed to the social role that is inherent to participants and patients in a clinical study comparing patients with healthy controls.

Furthermore, it is not clear yet whether it is the differential initial experimenter treatment or the group labeling alone that elicits the BP effect. We employed differential initial treatment to evoke negative expectations in patients whose typical clinical symptoms might be considered relatively inconsequential despite their impact on quality of life (Canonica, Mullol, Pradalier, & Didier, 2008). A similar procedure was employed by previous studies on patients with mild head injury (Suhr & Gunstad, 2002, 2005). Future studies should ascertain this effect in patients with a more severe clinical picture that renders such additional instructions unnecessary. Moreover, since differential treatment cannot be absolutely ruled out in patients with obvious ailments, future work might focus on the independent contributions of group labeling and experimenter treatment to the BP effect.

Our results clearly show that the knowledge of being a patient and the possible detriments entailed in this role can affect critical measures. This psychological component might lead to a systematic overestimation of the actual effects elicited by the disease in question. We propose that future patient studies should take care to avoid or minimize this confound. Possible strategies include a stronger emphasis on within-group comparisons of patients with graded symptom severity or a similar study design as was employed in this study by labeling patients as controls in an allegedly unrelated study. Another possibility would be to avoid solely comparing patient data with healthy controls in favor of inviting patients suffering from other diseases (Cornblatt, Lenzenweger, & Erlenmeyer-Kimling, 1989; Tsuang & Dempsey, 1979) as is already common in certain fields.

Author contributions

KAS had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design*: KAS, CB. *Acquisition of Data*: KAS. *Analysis and interpretation of the data*: KAS, RP, CB. *Drafting of the manuscript*: KAS, RP, CB. *Obtained funding*: CB. *Study supervision*: KAS, CB.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

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