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Relationship of prosthesis ownership and phantom limb pain: results of a survey in 2,383 limb amputees

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Abstract

Phantom limb pain (PLP) accounts for a significant reduction in quality of life and is difficult to treat. Prosthesis use has been shown to negatively co-vary with PLP. Recent research on body perception in amputees suggest that prosthesis ownership, defined as the extent to which a prosthesis is experienced as being part of the body rather than an artificial device foreign to the body, might interact with PLP. We used survey data from 2,383 unilateral prosthesis-using upper or lower limb amputees and performed regression analyses to determine the relationship between prosthesis ownership and PLP. To test for specificity, we examined the role of prosthesis ownership also for residual limb pain (RLP) and non-painful phantom limb sensations (npPLS). Prosthesis ownership was reduced in older participants and higher in lower compared to upper limb amputees. A longer residual limb and more frequent prosthesis use as well as a longer time since amputation also yielded higher values. Prostheses based on natural principles were associated with higher prosthesis ownership. PLP and RLP were lower with higher prosthesis ownership, and RLP but not PLP was lower when prosthesis use was frequent. There were no significant associations for npPLS. The regression results differ in some aspects from those revealed by univariate analyses, emphasizing the importance of multivariate statistical approaches. Our findings provide insights into the interplay of body-

and pain-related sensations after amputation, and could help to develop new treatment approaches for both PLP and RLP.

Keywords: phantom limb pain; residual limb pain; prosthesis use; prosthesis ownership

1. Introduction

After the amputation of a limb, the majority of amputees complains of phantom limb pain (PLP), where painful sensations are located in the removed limb [4,16,30,31,61]. PLP accounts for a significant reduction in health-related quality of life [64] and is difficult to treat [2]. The contributions of both peripheral [65] and central factors [19,20,38] to the development and maintenance of PLP have been discussed.

Prosthetic devices are used to at least partly restitute the amputee's body integrity. In upper limb amputees, prosthesis use, particularly the use of prostheses with extended functionality compared to those with restricted functionality, has been shown to negatively covary with both PLP (effect sizes (Cohen's *d*) of about 1.5 to 2.0 [36,66]) and accompanying dysfunctional alterations in cortical body representations [36]. These results suggest that prosthesis use has preserving effects on peripheral and/or central physiology, which might counteract the development or maintenance of chronic PLP.

Prosthesis use further affects the amputees' body perception. For example, using a prosthesis is associated with overestimation of residual limb length [43] and higher vividness of phantom limb sensations [26]. Giummarra et al. [22] reported that about 30% of limb amputees perceive that their phantom would either fuse with their prosthesis or disappear when they wore the device. These descriptions indicate that in some amputees the use of a prosthesis interacts with the perception of the body, which ultimately leads to the perception that the prosthesis becomes a part of the amputee's body [47]. However, amputees differ in the degree of prosthesis ownership, that is, 'the feeling that the physical body and its parts, such as its

hands and feet, belong to ‘me’ and are ‘my’ body’([5], page 556): while some amputees perceive the device merely as a tool not belonging to the body, others report that the device becomes an integral part of their physical selves [46]. This kind of experience has previously been identified as contributing significantly to bodily self-consciousness and can be assessed with interviews or questionnaires [15,35,46].

It has previously been proposed that the perception of an intact body might modulate deafferentation pain [41,55]. Thus, prosthesis ownership might have beneficial effects on PLP. However, until now, use-dependent and percept-dependent prosthesis contributions to PLP have not been differentiated. Moreover, there are inconsistent results: while one study [22] revealed no significant association between prosthesis incorporation and PLP, another study [30] reported that the percept of a prosthesis as merged with the body (versus the percept of a prosthesis as foreign part to the body) was associated with a significantly lower prevalence of PLP.

In the present study, we examined a large cohort of prosthesis-using unilateral upper or lower limb amputees and applied ordinal logistic regressions to determine the relationship of prosthesis ownership, frequency of prosthesis use, and PLP. In order to evaluate the specificity of the association, we also examined residual limb pain (RLP) and non-painful phantom limb sensations (npPLS). We expected prosthesis ownership to be specifically associated with reduced PLP, independent of frequency of prosthesis use.

2. Methods

Data base and sample description

In the context of the PHANTOMMIND project, we established a nationwide data base of upper and lower limb amputees. The participants completed a questionnaire that assessed demographic and amputation- and prosthesis-related information as well as phantom limb phenomena (cf., [4]). All participants gave written informed consent prior to being entered in

the data base and the study protocol adhered to both the Declaration of Helsinki and the Declaration of the World Medical Association. The study was approved by the Ethics Commission of the Medical Faculty Mannheim, Heidelberg University.

Sample description

At the time of the present analysis, the PHANTOMMIND data base included questionnaire data of 3,501 subjects with acquired unilateral major limb deficiency who were at least 18 years old. Congenital limb absence, more than one amputated limb, and minor amputations were exclusion criteria for the present study. All questionnaires had been checked for completeness and plausibility, and incomplete or implausible questionnaires had been completed or corrected via telephone interviews. Nevertheless, in the context of the present study, 368 participants had to be excluded because items remained incomplete or inconsistent. An additional 636 subjects stated not having a prosthesis or not having used it in the four weeks prior to study participation, and 67 participants had missing data in the measure of prosthesis ownership. Finally, 47 subjects had to be excluded due to being amputated before the age of 4 or uncertainty regarding this issue, since it has been suggested that the brain processes of amputated children below this age are different from persons who were amputated at an older age [44].

Thus, N = 2,383 prosthesis-using participants with acquired unilateral major limb amputation were included in the present analysis. The majority of participants were male (82.07%, two missing data). The mean age was 63.70 years (standard deviation (SD) = 15.78; range: 18 to 98 years). Detailed information on the clinical data of the sample is given in Table 1, and the type of used prostheses is given in Table 2.

Insert Table 1 about here

Insert Table 2 about here

Questionnaire

The questionnaire contained 53 items, and is a modified version of the Phantom and Stump Phenomena Interview [67]. For the present study, we used demographic data of the participants such as gender and age as well as amputation-related information, prosthesis-related features, and characteristics of painful and non-painful post-amputation phenomena related to the affected limb.

Amputation-related information: Participants were asked about the site (upper or lower limb) and side (left or right) of amputation. In an additional body drawing, the participants marked the level of amputation, which was used to calculate the length of the residual limb in %. We further used two items based on the Edinburgh Handedness Inventory [49] for assessing dominance of the lower or the upper limb prior to amputation: '*Which hand did you use for writing before being amputated?'* or '*Which leg did you use to kick an object, for example a ball, before being amputated?'*. Participants were asked to indicate *left*, *right*, or *both sides alike*. Upper limb amputees were additionally asked whether they were re-educated left-handers. Together with the actual side of amputation, we determined whether the dominant or non-dominant limb had been amputated. The amputated limb was considered non-dominant in the case of bilateral handedness or footedness; re-educated left-handers were considered left-handed before amputation. We further asked for the month and year of amputation, which was used to calculate the time since amputation in years together with the return date of the questionnaire. Finally, the participants were asked to provide the reason for amputation

(multiple responses allowed): accident, injury, infection, tumor, peripheral vascular disease, or other reasons.

Prosthesis-related information: The participants were asked what type of prostheses they used, using a list previously introduced in the Phantom and Stump Phenomena Interview [67]. Upper limb prostheses were further dichotomized according to the level of functionality (*restricted functionality* was assumed for prostheses that were characterized as cosmetic; *extended functionality* was assumed for prostheses that were characterized as myo-electric, body-powered, Sauerbruch, or hybrid prostheses; see Table 2). We further asked for the frequency of prosthesis use per week (0 – *not at all;* 1 – *less than twice;* 2 – *every second day;* 3 – *almost daily;* 4 – *daily*) and per day (0 – *never;* 1 – *one to two hours;* 2 – *several hours, but not throughout;* 3 – *half a day;* 4 – *from morning to evening*). By multiplying both ratings, we obtained an ordinally scaled prosthesis use frequency score ranging from 0 to 16 (10 ranks with the values 0, 1, 2, 3, 4, 6, 8, 10, 12, and 16, of which the first (value of 0) represents *no use* and the tenth (value of 16) represents *highly frequent use*; '0', however, was an exclusion criterion, see above). Finally, the participants were asked for their ownership experiences related to the prosthesis: *How much do you feel that the prosthesis is part of your body when you are wearing it?* We used a numerical rating scale ranging from 0 – *the prosthesis is foreign to my body* to 10 – *the prosthesis is merged with my body* (the captions of the poles were taken from [30]). Although the participants were asked to clearly check only one given number, some participants put a mark between the numbers; these were assigned to the next higher number, which was the case for less than 3% of participants. This measure is referred to as *prosthesis ownership.*

Presence and severity of post-amputation experiences: The participants were asked whether they had experienced PLP, RLP, and npPLS in the past three months (separate assessments). These post-amputation phenomena were briefly described, followed by the response alternatives a) *No, I have never experienced PLP/RLP/npPLS,* b) *No, I do not experience*

PLP/RLP/npPLS currently, but I did so in the past, and c) *Yes, I currently experience PLP/RLP/npPLS*. The first two response alternatives were pooled as *current absence* of the phenomenon, whereas the last response alternative was coded as *current presence*. The participants were then asked to indicate the average intensity of each phenomenon in the past four weeks, using a numerical rating scale ranging from 0 – *no pain / no sensations* to 10 – *intolerable pain / very strong sensations*. Again, values were rounded up to the next higher number if the participants put a mark between two values (which was the case for less than 5% of participants). In addition, the frequency of the respective phenomenon was assessed, using ordinal categories ranging from 1 to 9 (1 – *less than once a month*, 2 – *once a month*, 3 – *every two weeks*, 4 – *one to two times a week*, 5 – *at least three times a week*, 6 – *at least five times a week*, 7 – *once a day*, 8 – *several times a day*, 9 – *permanently*). Participants who stated that they did not experience a certain post-amputation phenomenon in the last three months were coded with a 0 in the intensity rating (i.e., no pain / sensation), and a 0 in the frequency rating (i.e., phenomenon did not appear in the last three months). We multiplied the intensity rating by the frequency rating, resulting in an ordinal *severity score* ranging from 0 to 90. For simplicity, we pooled the scores 1-10 to rank 1, 11-20 to rank 2, and so on, with the 0 retaining as its own rank, so that we obtained ten ranks for each post-amputation phenomenon ranging from 0 – *not present* to 9 – *most severe*.

Statistical analyses

First, we report descriptive statistics for prosthesis ownership, frequency of prosthesis use, and post-amputation phenomena severity. After inspection of the distributions of the target outcome variables, we expected the assessed data to be ordinal, not equidistant, and not normally distributed, so that classical linear regressions were not suitable. Instead, we fitted a cumulative logit model, also known as ordered logit model, proportional odds model, or ordinal logistic regression model, which is a natural extension of the logistic regression model

from binary responses to ordinal responses with more than two categories (Duncan & Dunn, 2002, https://support.sas.com/resources/papers/proceedings/proceedings/sugi27/p200-27.pdf). By applying this approach, we initially performed an ordinal logistic regression analysis (n = 2,258) on prosthesis ownership (eleven categories), including the regressors gender (0 = male, 1 = female), age (in years), site (0 = lower limb, 1 = upper limb) and side (0 = right, 1 = left) of the amputation, dominance of the amputated limb (0 = non-dominant limb, 1 = dominant limb), length of the residual limb (in %), time since amputation (in years), and frequency of prosthesis use (9 categories, from 1 – *rare* to 9 – *highly frequent*) (forced entry). With this analysis, we sought to identify variables which were significantly associated with prosthesis ownership. In two subsequent regression analyses for either upper (n = 257) or lower limb amputees (n = 1,368), we added prosthesis type as additional regressor, if the used prosthesis could be clearly categorized (see Table 2): 0 – *prostheses with restricted functionality* and 1 – *prostheses with extended functionality* for upper limb amputees; and 0 – *exoskeletal* and 1 – *modular* for lower limb prostheses. This dichotomization allowed us to examine the effects of prosthesis function (i.e., upper limb prostheses characterized by extended functionality and modular lower limb prostheses) on prosthesis ownership.

We report on univariate associations between prosthesis ownership (eleven categories) and frequency of prosthesis use (nine categories) with PLP and other post-amputation phenomena (ten categories) using Spearman correlations (Bonferroni-corrected p-values for six comparisons, i.e., p_{Bonf}). In order to analyse the association between both prosthesis ownership and frequency of prosthesis use and the absence/presence of post-amputation phenomena, we employed X^2 tests. For this purpose, we dichotomized the sample according to current absence (severity rank = 0) and current presence (severity rank > 0) of the respective phenomenon. We report on the X^2 statistics, p_{Bonf}, and Cramer's V as a measure of association strength.

We then entered (forced entry) the variables that were significantly associated with prosthesis ownership into three separate ordinal logistic regression analyses (n = 2,079 each) on a) PLP severity, b) RLP severity, and c) npPLS severity (ten categories each). Since there is evidence that the intra-individual prevalence of different post-amputation phenomena is significantly related [28,60], for each of these models, we controlled for the other two phenomena, i.e., in the regression analysis for PLP, we entered RLP and npPLS, in the regression analysis for RLP, we entered PLP and npPLS, and in the regression analysis for npPLS, we entered PLP and RLP as regressors. This approach permitted us to control for shared variation between post-amputation phenomena.

For the logit models, it was assumed that the effect of an explanatory variable is identical for all modelled logits (known as the assumption of proportional odds [1]). In order to assess the equal slopes assumption [42], which corresponds to the proportional odds assumption in the models, we used the score test and graphical techniques such as plotting the empirical logits. If there was evidence for violating the proportional odds assumption (e.g., by not finding at least roughly parallel curves for the empirical logits), we fitted a partial proportional odds model allowing for non-proportionality in the respective regressor variable(s), which is indicated by degrees of freedom (*df*) larger than 1. Thus, we avoided the violation of basic assumptions for our models. For the regression models, we provide the test statistic (Wald X^2), *p*-values, and the estimate as well as the 95% confidence interval of odds ratios (*OR*). Due to relative redundancy of the models (caused by sub-analyses for prosthesis ownership and repeated control of post-amputation phenomena), we applied Bonferroni-correction to the models' statistics (by multiplying the *p*-values by 3).

Regression analyses were carried out with SAS v9.4 (SAS, Cary, NC, USA), all other statistical analyses were performed with IBM SPSS v25.

3. Results

Prosthesis use and prosthesis ownership

The amputees reported a high frequency of prosthesis use (median (*Mdn)* = 9.00, interquartile range (*IQR*) = 1.00), with about 75% reporting the highest rank (i.e., daily use, from morning to evening, see Figure 1a; and Supplementary Table S1, available at http://links.lww.com/PAIN/B168). The amputees showed a large variation in prosthesis ownership experiences (Figure 1b; and Supplementary Table S1, available at http://links.lww.com/PAIN/B168). The central tendency of data (*Mdn* = 7.00, *IQR* = 4.00) indicates that the majority of limb amputees have rather high levels of prosthesis ownership, with almost 59% reporting prosthesis ownership higher than 5 (representing the middle of the continuum). Only a minority of less than 7% denied any ownership experiences for their prosthesis.

Phantom limb pain and other post-amputation phenomena

Most participants had rather moderate severity levels of post-amputation phenomena (*Mdn* = 1.00, *IQR* = 3.00 for PLP and RLP; *Mdn* = 1.00, *IQR* = 4.00 for npPLS). At least one third of participants had a rank of 0 each, i.e., they reported the current absence of the phenomena. The data are visualized in Figure 2 and given in detail in Supplementary Table S1 (available at http://links.lww.com/PAIN/B168).

Insert Figure 1 about here

Insert Figure 2 about here

Regression on prosthesis ownership

Gender, side of amputation, and dominant vs non-dominant limb amputation had no significant relationship with prosthesis ownership. Site of amputation (0 = lower limb amputation; 1 = upper limb amputation), however, was significantly correlated with prosthesis ownership (OR = 0.76; p = .002), indicating that lower limb amputees experienced higher prosthesis ownership compared to upper limb amputees. Age was significantly negatively related to prosthesis ownership (OR = 0.97; p < .001), indicating that the younger the amputee, the more the prosthesis was perceived as belonging to the body. The length of the residual limb was significantly positively related to prosthesis ownership (OR = 1.01; p < .001), that is, the longer the residual limb, the stronger the experience of ownership for the prosthesis. Prosthesis ownership was more intense when the amputation dated back longer (OR = 1.02; p < .001). Finally, we found a strong and significant positive relationship between the frequency of prosthesis use and ownership for the prosthesis, with an OR of 1.39 (p < .001). Statistical details are given in Table 3, and significant relationships are further visualized in a univariate fashion in Figure 3. In total, the model was significant (Wald X^2_8 = 455.32, p_{Bonf} < .001) and explained 20.4 % of the variation in prosthesis ownership.

Since site of amputation was significantly related to prosthesis ownership, we individually repeated the regression analysis for upper and lower limb amputees by including type of prosthesis as additional regressor. These analyses revealed a similar pattern of results (both models were significant, Wald X^2_8 = 281.41, p_{Bonf} < .001 for lower limb amputees, and Wald X^2_8 = 74.88, p_{Bonf} < .001 for upper limb amputees), with the length of the residual limb, time since amputation, and frequency of prosthesis use being significantly positively related to prosthesis ownership in both upper and lower limb amputees (all $OR \geq 1.02$; all p < .05). Age was significantly negatively associated with prosthesis ownership only in lower limb

amputees (*OR* = 0.97; $p < .001$). Interestingly, prosthesis type emerged as significant regressor in both models, with upper limb prostheses with extended (compared to restricted) functionality or modular (compared to exoskeletal) lower limb prostheses being significantly associated with higher prosthesis ownership (*OR* = 1.29 for lower limb amputees and *OR* = 2.02 for upper limb amputees; both $p < .05$). Details of these additional analyses are provided in Supplementary Tables S2 and S3 (available at http://links.lww.com/PAIN/B168).

Insert Table 3 about here

Insert Figure 3 about here

Univariate relationships between prosthesis ownership, frequency of prosthesis use, and post-amputation phenomena

Using Spearman correlations, we found that both prosthesis ownership (all $\rho \geq -.11$, all $p_{Bonf} < .001$) and frequency of prosthesis use (all $\rho \geq -.08$, all $p_{Bonf} < .001$) correlated significantly negatively with PLP and the other post-amputation phenomena. Details of these relationships are given in Table 4. We further analysed the percentages of participants who reported absence (i.e., a severity rank of 0) or presence (i.e., a severity rank > 0) of post-amputation phenomena and the univariate relationship with both prosthesis ownership and frequency of prosthesis use. Prosthesis ownership was significantly related to the absence of PLP ($X^2_{10} = 106.22$, $p_{Bonf} < .001$, Cramer's $V = .22$) and RLP ($X^2_{10} = 42.92$, $p_{Bonf} < .001$, Cramer's $V = .14$), but not npPLS ($X^2_{10} = 22.90$, $p_{Bonf} = .071$, Cramer's $V = .10$). Frequency of prosthesis use

was also significantly related to the absence of PLP (X^2_8 = 25.81, p_{Bonf} = .005, Cramer's V = .11), but not RLP (X^2_8 = 8.00, p_{Bonf} = 1.000, Cramer's V = .06) or npPLS (X^2_8 = 14.10, p_{Bonf} = .470, Cramer's V = .08). The associations for PLP and RLP are visualized in Figure 4.

Insert Table 4 about here

Insert Figure 4 about here

Regression of prosthesis ownership on phantom limb pain and other post-amputation phenomena

In order to control for associations with prosthesis ownership, significant regressor variables revealed by the first analysis described above were also entered in the subsequent regression analyses on PLP and other post-amputation phenomena. All three models were significant (Wald X^2_{24} = 657.78, p_{Bonf} < .001 for PLP; Wald X^2_{24} = 336.79, p_{Bonf} < .001 for RLP; and Wald X^2_{24} = 446.02, p_{Bonf} < .001 for npPLS). All other statistics are provided in Table 5. We found that prosthesis ownership was significantly negatively related to both PLP and RLP (both p < .001), indicating that higher prosthesis ownership was associated with lower PLP and RLP, with comparable *ORs* of about 0.92 each. This was not true for npPLS, which showed no significant relationship with prosthesis ownership (*OR* = 0.98; p = .294). While there was a significant negative relationship between the frequency of prosthesis use and RLP severity (*OR* = 0.94; p = .023), frequency of prosthesis use did not emerge as individual significant regressor on PLP (*OR* = 1.01; p = .812). The same held for npPLS (*OR* = 0.98; p = .496).

Residual limb length was related to both PLP and RLP, but in a different direction each: while residual limb length had a negative relationship with PLP (*OR* = 0.99; $p < .001$), there was a positive association for RLP (*OR* = 1.01; $p < .001$). Lower limb amputation (coded as 0, compared to upper limb amputation, coded as 1) was related to both higher PLP (*OR* = 0.69; $p = .006$) and higher RLP (*OR* = 0.58; $p < .001$), while npPLS were significantly higher in upper limb amputees (*OR* = 1.53; $p < .001$). The older the participants, the more PLP was reported (*OR* = 1.02; $p < .001$); however, for RLP (*OR* = 0.99; $p = .013$) and npPLS (*OR* = 0.98; $p < .001$), there was an inverse relationship to age. Time since amputation was negatively associated with PLP (*OR* = 0.98; $p < .001$) and positively associated to RLP (*OR* = 1.02; $p < .001$), while there was no significant association for npPLS. Post-amputation phenomena were moderately to highly positively interrelated, although detailed analyses on the partial proportional odds revealed large variation. There was evidence for violating the proportional odds assumption when controlling for the other two post-amputation phenomena in each of the three models. This is why we fitted a partial proportional odds model allowing for non-proportionality in the respective regressors (indicated by $df > 1$). Therefore, we present the results for these regressors in detail (in parentheses) in Table 5 as well. The explained variation for each model was moderate, with R^2 ranging between 13.9 % and 29.4 %.

Insert Table 5 about here

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4. Discussion

The experience that we are inextricably linked with our body is an essential feature of everyday life, with body ownership being one of the most relevant aspects [5,35]. Previous studies (e.g., [7,8,37]) revealed the importance of body ownership for psychological functioning by using the rubber limb illusion [6,11] and similar paradigms for the experimental manipulation of ownership experiences (for a review see [57]). Given that impaired physical integrity in amputees does not suspend the normal processes underlying bodily self-consciousness [15], it has been assumed that prosthesis ownership might be important for establishing prosthesis satisfaction [47].

Drawing on the data of a large cohort of prosthesis-using limb amputees, the present study investigated prosthesis ownership and its associations with phantom limb pain (PLP), residual limb pain (RLP), and non-painful phantom limb sensations (npPLS) using ordinal logistic regression analyses. We found large variation in prosthesis ownership, which was negatively associated with age and positively associated with lower (compared to upper) limb amputation, residual limb length, time since amputation, and frequency of prosthesis use. The negative association between age and prosthesis ownership matches results indicating that older non-amputated people show reduced proneness to the experimental manipulation of body ownership [18,29], which has been associated with age-related alterations in the capability for multimodal integration, although this finding is not unambiguous [39,51]. However, exposure to the prosthetic device seems to counteract the diminishing effects of age, since time since amputation as well as frequency of prosthesis use were positively associated with prosthesis ownership. The differences between upper and lower limb amputees might be related to a different level of attention to or salience of the device, while the positive association between prosthesis ownership and residual limb length might highlight the importance of limb-centered peripersonal space dimensions for eliciting ownership sensations [32], whose extent has been shown to be reduced for the affected limb

in amputees [9]. Interestingly, certain types of prostheses (that is, upper limb prostheses with extended functionality and lower limb prostheses emulating the skeletal structure of the leg) were associated with higher prosthesis ownership, suggesting that devices based on natural principles of functioning facilitate the perception of prosthesis ownership. These findings might prospectively help to better operationalize prosthesis ownership and related concepts in order to integrate inconsistent results (e.g., [22,30]).

The main aim of the present study was the elucidation of the relationship between PLP and prosthesis ownership. Univariate correlations revealed that both prosthesis ownership and the frequency of prosthesis use were significantly negatively associated with the severity of post-amputation phenomena. For prosthesis ownership, this univariate association was also found for the percentage of pain-free participants: about one out of four participants, who reported minimum prosthesis ownership, was PLP-free, while this was the case for more than half of the participants who reported maximum prosthesis ownership (+ 98%), supporting previous results [30]. For RLP, this effect was also present, but smaller in extent (+ 44%).

Controlling for other variables using ordinal logistic regressions, we found that higher levels of prosthesis ownership were significantly related to lower PLP and RLP, while npPLS were not significantly associated with prosthesis ownership. The association of prosthesis ownership with PLP was independent of the frequency of prosthesis use. This is an important finding, since it emphasizes that the amputee's perception, rather than the mere use of the prosthesis, is associated with PLP, and that univariate analyses might fail to consider the interactions between frequency of prosthesis use and prosthesis ownership. In contrast to PLP, RLP was related to the frequency of prosthesis use, independent of prosthesis ownership, in accordance with the finding that medical problems of the residual limb can interfere with prosthesis use [12].

It has been suggested that a correction of body perception may modulate PLP. Mirror therapy is a non-pharmacological treatment in which unilateral amputees are guided to perform

movements with their intact limb in front of a sagittally placed mirror and are encouraged to relate the visual image as much as they can to their phantom limb [54]. This kind of treatment has been shown to be effective for PLP [10]. Interestingly, experiences related to the mirrored limb have been identified as predictor for treatment success: the more participants are able to relate the visual image to their phantom, the less PLP they report after a treatment period of four weeks [21]. Although this finding as well as the present results are of correlative nature, there might be a causal relationship. It has been shown that the experimental induction of ownership in terms of the rubber limb illusion can reduce acute pain perception [17,25,48], although there are contrary findings [3,45]. As Martini [40] emphasized, perceived co-location of the real and the artificial limb might be necessary for the analgesic ownership effect, since it seems to be linked to visually induced analgesia occurring when one's own (but not another person's) observed body is painfully stimulated [33]. These results indicate that ownership experiences for artificial body parts that are located within the boundaries of peripersonal space might be important for the analgesic outcome, which has been shown to rely on the enhancement of effective connectivity between the visual body network and areas involved in pain processing [34], probably resulting in increased intracortical inhibition [23]. Visual analgesia has been empirically described for patients with chronic back pain [14], and has also been proposed to be of relevance for PLP treatment [58]. It has been suggested that the restoration of disturbed central visuo-motor loops might represent a potential target for the treatment of deafferentation pain [62]. In accordance with this view, there is evidence for a relationship between central visuo-motor connectivity, the neural processing of images of functional prostheses, and prosthesis use [63], suggesting a possible role for the motor system in the use-dependent visual representation of prostheses. We suggest that prosthesis ownership might have an enhancing effect on brain processes associated with analgesia of chronic PLP. Whether or not the perception of prosthesis ownership might further *prevent* the

development of PLP, particularly when the prosthetic device is implemented in an early stage after amputation, remains speculative.

Our results not only revealed a significant relationship between prosthesis ownership and PLP, but also for RLP. Interestingly, non-painful phantom limb sensations were unrelated to prosthesis ownership, although they showed significant associations to PLP and RLP (cf., [28,60,61]). This indicates that the found prosthesis ownership effect is specific for post-amputation pain, although not necessarily for PLP.

This study has several strengths and limitations. We carefully selected participants and included a large sample, so that generalizability of our results can be assumed. However, it should be mentioned that the vast majority of the present participants suffered from lower limb amputation which is compatible with the fact that a) leg amputations outnumber the amputations of arms, and that b) leg amputees, compared to arm amputees, more frequently use a prosthesis (e.g., [4,53]). Moreover, the sample displays heterogeneity regarding the reasons of limb loss, such as elective or traumatic amputations. Whether or not these factors are accompanied by different neural processes related to variation in pain and prosthesis ownership remains open. Furthermore, prosthesis ownership was assessed with only one previously introduced item targeting perceptual incorporation of the device [30], whose validity in terms of prosthesis embodiment [35,46,47] and/or bodily self-consciousness [5] has yet to be confirmed in prospective studies, also by using behavioral or other recently developed implicit measures (e.g., [27,59]). It has previously been shown that the incorporation of a non-body object involves other dimensions than ownership, such as agency (the sense of being in control of a body part) and spatial limb representation [35], which might also be of relevance for the embodiment or prostheses. How these other dimensions relate to PLP, and whether or not they show differential relationships to post-amputation phenomena, remains unknown. In this context, other prosthesis-related features should be considered as well. Desmond et al. [13] identified satisfaction with a prosthesis as significant predictor for

the severity of post-amputation pain. It can be assumed that prostheses that are perceived as belonging to the body are also accompanied by higher levels of prosthesis satisfaction, although this has not yet been empirically tested. Thus, it remains open how these factors are interrelated and whether or not they independently relate to PLP. Although there is evidence that the induction of ownership for artificial body parts can influence chronic pain, as described above, the conclusions that can be drawn from the present data are of correlative nature. Thus, the presence of pain could also reduce the flexibility of central body representations (cf., [56]) which might interfere with the experience of prosthesis ownership. Although the direction of effects has to be examined in prospective studies, there is some evidence that more naturalistic prosthetic devices equipped with sensory feedback both enhance prosthesis ownership experiences (e.g., [52]) and reduce PLP levels [50]. Identification of the underlying mechanisms of the relationship of pain, prosthesis use, and body perception could facilitate the development of better prosthetic devices that potentially reduce post-amputation pain.

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Figure captions

Figure 1: Prosthesis use and prosthesis ownership. a) Rank distribution for frequency of prosthesis use (*N* = 2,383 upper or lower limb amputees). Given is the percentage (left y-axis) and the absolute number of participants (*n*; right y-axis) for the reported frequency of prosthesis use (x-axis, rank from 1 – *rare* to 10 – *frequent*); b) rank distribution for prosthesis ownership (*N* = 2,383 upper or lower limb amputees). Given is the percentage (left y-axis) and the number of participants (*n*; right y-axis) reporting a given rank of prosthesis ownership (from 0 – *prosthesis is perceived as foreign to the body* to 10 – *prosthesis is perceived as merged with the body*).

Figure 2: Rank distribution of severity of post-amputation phenomena in the included sample of upper or lower limb amputees. Given are the valid percentages for phantom limb pain (*n* = 2,270), residual limb pain (*n* = 2,293), and non-painful phantom limb sensations (*n* = 2,243) from 0 – *not present* to 9 – *most severe*.

Figure 3: Univariate associations between prosthesis ownership and variables identified as being significantly associated with prosthesis ownership in the ordinal logistic regression analysis. Continuous variables (i.e., a) age of the participants, b) time since amputation, and c) residual limb length) were split in deciles each; note that the numbers in parentheses under deciles represents the range covered by the respective decile. Discrete variables are given in d) (site of amputation; i.e., lower or upper limb) and e) (frequency of prosthesis use). Provided are box plots with medians and interquartile ranges (*IQR*), whiskers represent a maximum data range of 1.5 × *IQR*. Outliers and extreme values are not denoted.

Figure 4: Associations between reported absence of phantom limb pain (i.e., a severity rank of 0) and a) prosthesis ownership and b) frequency of prosthesis use, or absence of residual limb pain (again a severity rank of 0) and c) prosthesis ownership and d) frequency of prosthesis use. Note that prosthesis ownership (minimum = prosthesis ownership of 0; low = prosthesis ownership of 1-3; medium = prosthesis ownership of 4-6; high = prosthesis ownership of 7-9; maximum = prosthesis ownership of 10) and frequency of prosthesis use (low to medium = ranks 1-8; high = rank 9) were newly categorized for illustrative purposes); provided are the respective percentages, which are explicitly given at the upper end of each bar; the number at each bar's base denotes the valid number of participants for the respective category.

Tables

Table 1: Clinical information of the sample (*N* = 2,383). *n* = number; *M* = mean; *SD* = standard deviation.

Limb amputation (categorical data)	***n***	**%**	***n* missing data**
Lower limb amputation	2,060	86.45	0
Left-sided amputation	1,312	55.06	0
non-dominant limb amputation	1,331	58.87	122
Limb amputation (continuous data)	***M***	***SD***	***n* missing data**
time since amputation (years)	30.97	22.56	0
residual limb length (%)	42.37	19.04	3
Prevalence of post-amputation phenomena	***n***	**%**	***n* missing data**
Phantom limb pain	1,467	63.70	80
Residual limb pain	1,209	52.38	75
non-painful phantom phenomena	1,362	58.37	48
Reason for amputation (multiple responses allowed)	***n***	**%**	**no missing data**
accident	1,302	54.64	---
injury	302	12.67	---
infection	232	9.74	---
cancer	211	8.85	---
peripheral vascular disease	356	14.94	---
other reasons	478	20.06	---

Table 2: Used prostheses of upper or lower limb amputees (multiple responses allowed if more than one prosthesis was owned; valid *n* = 2,306); *n* = number.

upper limb amputees (*n* = 322)			**lower limb amputees (*n* = 1984)**		
Prosthesis type	***n***	**%**	**Prosthesis type**	***n***	**%**
cosmetic	165	51.24	exoskeletal	642	32.36
myo-electric	117	36.34	modular	851	42.89
body-powered	43	13.35	interim	62	3.13
Sauerbruch	8	2.48	early care	42	2.12
hybrid	4	1.24	----		
other	39	12.11	other	411	20.72
prostheses with restricted* / extended** functionality[a]	126 / 134	39.13 / 41.61	exoskeletal / modular prostheses[a]	609 / 820	30.70 / 41.33

* cosmetic prostheses; ** myoelectric, body-powered, Sauerbruch, or hybrid prostheses; [a] only persons with one prosthesis type; persons with several types of prostheses, where restricted/extended functionality and exoskeletal/modular construction could not be clearly determined, were excluded here

Table 3: Ordinal regression analyses on prosthesis ownership in *n* = 2,258 limb amputees.

Effect	**df**	**Wald X^2**	**OR estimate**	**Wald 95% CI for OR**	***p*-value**
gender[a]	1	0.016	0.988	0.814-1.198	.901
age	1	83.518	0.974	0.969-0.980	< .001
site[b]	1	5.939	0.757	0.606-0.947	.015
side[c]	1	0.137	0.960	0.772-1.194	.712
dominant limb amputation[d]	1	0.741	0.907	0.727-1.132	.389
residual limb length	1	29.451	1.011	1.007-1.015	< .001
time since amputation	1	96.971	1.021	1.017-1.025	< .001
frequency of prosthesis use	1	200.805	1.387	1.326-1.451	< .001
R^2	.204				

[a] 0 = male, 1 = female; [b] 0 = leg, 1 = arm; [c] 0 = right, 1 = left; [d] 0 = amputation of the non-dominant limb, 1 = amputation of the dominant limb; CI = confidence interval; df = degrees of freedom; R^2 = explained variation, OR = odds ratio

Table 4: Univariate Spearman correlation coefficients (ρ, with degrees of freedom) and Bonferroni-corrected p-values (p_{Bonf}) for the relationship between prosthesis ownership or frequency of prosthesis use and post-amputation phenomena. PLP = phantom limb pain; RLP = residual limb pain; npPLS = non-painful phantom limb sensations.

	PLP severity		RLP severity		npPLS severity	
	$\rho_{2,268}$	p_{Bonf}	$\rho_{2,291}$	p_{Bonf}	$\rho_{2,241}$	p_{Bonf}
Prosthesis ownership	-.263	< .001	-.164	< .001	-.111	< .001
Frequency of prosthesis use	-.158	< .001	-.082	< .001	-.097	< .001

Table 5: Ordinal logistic regression analyses on PLP and other post-amputation phenomena reported by *n* = 2,079 upper or lower limb amputees. PLP = phantom limb pain; RLP = residual limb pain; npPLS = non-painful phantom limb sensations; CI = confidence interval; *df* = degrees of freedom; R^2 = explained variation; [a] 0 = lower limb, 1 = upper limb; *OR* = odds ratio; *PPO* = partial proportional odds.

	PLP severity					**RLP severity**					**npPLS severity**				
Regressor	*df*	Wald X^2 (range for *PPO*)	*OR* estimate (range for *PPO*)	Wald 95% CI for *OR* (range for *PPO*)	*p*-value (range for *PPO*)	*df*	Wald X^2 (range for *PPO*)	*OR* estimate (range for *PPO*)	Wald 95% CI for *OR* (range for *PPO*)	*p*-value (range for *PPO*)	*df*	Wald X^2 (range for *PPO*)	*OR* estimate (range for *PPO*)	Wald 95% CI for *OR* (range for *PPO*)	*p*-value (range for *PPO*)
prosthesis ownership	1	31.154	0.916	0.888-0.945	< .001	1	25.333	0.924	0.896-0.953	< .001	1	1.102	0.983	0.953-1.015	.294
age	1	56.671	1.024	1.018-1.030	< .001	1	6.201	0.992	0.986-0.998	.013	1	50.003	0.978	0.972-0.984	< .001
site [a]	1	7.719	0.688	0.529-0.896	.006	1	18.639	0.563	0.433-0.731	< .001	1	11.662	1.534	1.200-1.961	< .001
residual limb length	1	29.334	0.988	0.984-0.992	< .001	1	14.590	1.009	1.004-1.013	< .001	1	2.648	0.996	0.992-1.001	.104
time since amputation	1	97.965	0.978	0.973-0.982	< .001	1	43.530	1.016	1.011-1.021	< .001	1	3.770	0.996	0.991-1.000	.052
frequency of prosthesis	1	0.057	1.006	0.957-1.057	.812	1	5.160	0.944	0.898-0.992	.023	1	0.464	0.983	0.936-1.033	.496

use															
PLP severity	-----	-----	-----	-----	-----	9	161.951 (23.268-118.745)	(1.145-1.410)	(1.096-1.197 to 1.226-1.621)	< .001 (all < .001)	9	250.576 (33.058-183.240)	(1.258-1.409)	(1.200-1.320 to 1.341-1.481)	< .001 (all < .001)
RLP severity	9	205.786 (16.823-122.955)	(1.100-1.431)	(1.051-1.152 to 1.273-1.610)	< .001 (all < .001)	-----	-----	-----	-----	-----	9	36.086 (0.031-17.433)	(0.991-1.104)	0.892-1.100 to 1.054-1.157)	< .001 (< .001-.861)
npPLS severity	9	208.364 (4.647-152.985)	(1.132-1.352)	(1.011-1.267 to 1.289-1.418)	< .001 (< .001-.031)	9	17.349 (0.152-12.411)	(1.026-1.087)	(0.901-1.169 to 1.038-1.139)	.044 (< .001-697)	-----	-----	-----	-----	-----
R^2	.294					.139					.195