Does Familial Aggregation of Chronic Low Back Pain Affect Recovery?

A Population-Based Twin Study

Joshua R. Zadro, BappSc (PT, Hons), * Debra Shirley, PhD, * Juan F. Sánchez-Romera, PhD, †, ‡, ‡ ‡ Juan R. Ordoñana, PhD, †, ‡, ‡ and Paulo H. Ferreira, PhD *

Study Design. Longitudinal twin-cohort study.
Objective. To investigate the effect familial aggregation of chronic low back pain (LBP) has on the recovery from chronic LBP.
Summary of Background Data. LBP is a worldwide problem, with pain and disability often becoming chronic. Genetics and familial behaviors could significantly affect the recovery from chronic LBP but have not been extensively investigated.
Methods. A total of 624 Spanish twins from the Murcia Twin Registry reported experiencing chronic LBP within the past 2 years during the 2009/11 data collection wave and were followed up in 2013. Familial aggregation of chronic LBP was determined by the co-twin experiencing chronic LBP within the past 2 years at baseline. Twins reporting LBP “within the past 4 weeks” at follow-up were considered to have not recovered.
Results. There were 455 twins with available data on LBP at follow-up and available data on LBP from their co-twin at baseline. Twins with an affected co-twin at baseline were significantly more likely to have not recovered from chronic LBP at follow-up (odds ratio [OR] = 1.6, 95% confidence interval [CI]: 1.0–2.4, \( P = 0.046 \)). This relationship was stronger for monozygotic twins (OR = 2.5, 95% CI: 1.3–4.8, \( P = 0.006 \)) (n = 172) but disappeared when considering only dizygotic twins (OR = 1.1, 95% CI: 0.6–2.0, \( P = 0.668 \)) (n = 283). Sibling-relative recurrence risk (\( \lambda_s \)) was 1.2 for the total sample, 1.5 for monozygotic twins, and 1.1 for dizygotic twins.
Conclusion. Having a sibling with chronic LBP at baseline increased the likelihood of LBP at follow-up by 20%, with this likelihood increasing to 50% if the sibling was an identical twin. These results are novel and highlight the important influence genetics have on people’s recovery from chronic LBP. Information regarding the presence of chronic LBP within a family is easy to obtain and has the potential to inform clinicians on which patients are less likely to recover when treatment implementation is not considered.
Key words: chronic low back pain, dizygotic twins, familial aggregation, monozygotic twins, Murcia Twin Registry, prospective, recovery, relative recurrence risk, siblings, twin study.

Level of Evidence: 3
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Disability resulting from low back pain (LBP) is a worldwide problem. Although most people improve within the first 6 weeks after an episode of LBP, many fail to completely recover, with pain and disability becoming chronic. Numerous factors have been investigated in the recovery from chronic LBP with only a few demonstrating a consistent negative effect, including a previous history of LBP and longer symptom duration. The effect of familial factors on the recovery from chronic LBP has, however, not been analyzed.

Genetics have been shown to account for up to 67% of chronic LBP cases, with the family environment accounting for up to 41% of chronic LBP cases. Therefore, among familial factors that could influence the recovery from chronic LBP, familial aggregation of chronic LBP is likely to be relevant. Familial aggregation of chronic LBP is associated with the presence of chronic LBP in adults, whereas having family members suffering from chronic LBP increases the likelihood of developing chronic LBP and displaying high fear avoidance beliefs about LBP. Despite this, familial aggregation of chronic LBP is yet to be investigated in the recovery from chronic LBP.
Understanding how familial aggregation of chronic LBP affects the recovery from chronic LBP will help clinicians identify those at risk of poor outcomes and potentially inform the direction of treatment. This will help extend the understanding of factors affecting recovery from chronic LBP beyond the individual and toward family. Hence, the aim of the present study is to investigate the effect familial aggregation of chronic LBP has on recovery from chronic LBP, while gaining insights into the influence of genetics and the environment.

MATERIALS AND METHODS

Participants and Data Collection
The sample for this longitudinal study was drawn from the Murcia Twin Registry (MTR), a population-based registry of adult twins born between 1940 and 1966 in the region of Murcia, Spain. Detailed information about sample recruitment practices and characteristics of the MTR can be found elsewhere. Data were collected through a health-related questionnaire via face-to-face or phone interviews in three consecutive data waves: 2007, 2009/11, and 2013. The second data collection wave (2009/11) was performed in consecutive years for female-female pairs, male-male pairs, and opposite sex pairs in 2009, 2010, and 2011, respectively. The health-related questionnaire included information on demographics, basic health history, and lifestyle factors. Data from the 2009/11 and 2013 collection waves formed the basis of the analyses. We decided not to use data from the 2007 collection wave as limited data on LBP were collected from a smaller number of female-female pairs. Assessors were blinded to the predictor and outcomes of the present study. All registry and data collection procedures used in the MTR have been approved by the Committee of Research Ethics of the University of Murcia.

There were 2148 twins between 43 and 71 years old who provided information regarding LBP status at baseline by responding to the following question: “Have you ever suffered from chronic LBP?” Chronic LBP was considered as the presence of LBP lasting for 6 months or longer, including seasonal or recurrent episodes, and was clearly outlined to participants by a researcher involved in data collection. Those who answered “yes” were asked a follow-up question: “Have you experienced chronic LBP in the last 2 years?” There were 624 twins who answered “yes” to both questions and were included in this longitudinal analysis (Figure 1).

Figure 1. STROBE flow diagram. DZ indicates dizygotic; LBP, low back pain; MZ, monozygotic.
Zygosity Ascertainment

Zygosity was ascertained by a 12-item questionnaire focusing on the degree of similarity and mistaken identity between twins. This questionnaire correlates with zygosity determined by DNA in approximately 96% of the cases.\(^{(11)}\)

Assessment of Recovery From Chronic Low Back Pain

Questions regarding LBP status at follow-up were adapted from standardized definitions developed to facilitate comparison across epidemiological studies.\(^{(12)}\) Participants who had experienced chronic LBP in the last 2 years were asked the following question at follow-up: “When was the last time you experienced LBP?” Participants who selected “within the past 4 weeks” were considered to have not recovered from chronic LBP. This definition is based on the best available evidence, suggesting being pain-free for the duration of a month is sufficient to infer recovery.\(^{(13)}\)

Assessment of Familial Aggregation of Chronic Low Back Pain

Familial aggregation of chronic LBP (predictor variable) was determined by the co-twin suffering from chronic LBP within the past 2 years at baseline.

Assessment of Covariates

We selected potential confounders based on previous literature and data availability including: age, sex, body mass index, smoking, sedentary behavior, symptoms of depression/anxiety, and sleep quality. Data on body mass index were either self-reported (67.4%) or objectively measured (32.6%). Data on smoking and sedentary behavior were based on the Spanish National Health Survey Questionnaire.\(^{(14)}\) Smoking was dichotomized as ex-smoker/never smoked or current smoker. Sedentary behavior was determined by participants’ engagement in leisure and daily physical activities. Leisure physical activity was assessed by participants selecting one of the following options: (i) I do not practice exercise. My leisure time is mostly sedentary (reading, watching TV, movies, etc.); (ii) sport or physical activity occasionally (walking, gardening, soft gym, light efforts, etc.); (iii) regular physical activity several times a month (tennis, jogging, swimming, cycling, team sports, etc.); (iv) physical training several times a week. Responses were dichotomized as no physical activity/sedentary (i) or occasional/regular physical activity (ii, iii, and iv). Daily physical activity was assessed by participants selecting one of the following options: (i) sitting most of the time; (ii) standing. No big movements or effort; (iii) walking, carrying light weights, moving but no big effort; (iv) tasks that require physical effort. Responses were dichotomized as no/low physical activity engagement (i and ii) or moderate/vigorous physical activity engagement (iii and iv). Participants who had engaged in no leisure physical activity and no/low daily physical activity were considered sedentary. Symptoms of depression/anxiety were assessed by participants selecting one of the following options based on the depression/anxiety domain of the EuroQol-5 dimension: (i) I am not anxious or depressed; (ii) I am moderately anxious or depressed; (iii) I am extremely anxious or depressed. Responses were dichotomized as not depressed or anxious (i) or moderately/extremely depressed or anxious (ii and iii). Sleep quality was assessed by participants’ score on the Spanish version of the Pittsburgh Sleep Quality Index. Responses were dichotomized as poor sleep quality (score ≥5) or good sleep quality (score ≤5).\(^{(15)}\)

Analysis

First, we conducted analyses to identify whether familial aggregation of chronic LBP affected the recovery from LBP. Univariate logistic regressions were performed to identify possible confounders that should enter the multivariate logistic regression models. Covariates were included in multivariate models if the P values from the univariate relationship between the covariables, and both the predictor and outcome were <0.2. Because baseline data were collected between 2009/11 we adjusted all analyses for follow-up length. Twin pairs were considered as clusters to account for their nonindependence.

To gain insights into the role of genetics as a familial predictor of recovery, we stratified analyses by zygosity. Dizygotic (DZ) twins share on average 50% of their segregating genes, whereas monozygotic (MZ) twins share approximately 100% of their segregating genes.\(^{(16)}\) Therefore, if the association is similar between analyses regardless of zygosity, this is likely to suggest that genetics are less influential as a familial predictor of recovery. If the magnitude of the association is, however, higher for MZ twins, this is likely to suggest that genetics play an important role as a familial predictor of recovery. Analyses were conducted using STATA statistical software (version 13.1) with the significance level set at 0.05. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the regression models.

Second, we calculated the sibling recurrence relative risk (\(\lambda_s\)). For our study, \(\lambda_s\) represents the risk of nonrecovery from chronic LBP in the presence of an affected sibling (chronic LBP at baseline), compare to the risk of nonrecovery in the total sample (population prevalence). This is a commonly reported measure of familial aggregation, and has been adapted to reduce the bias when considering conditions with a high prevalence (e.g., LBP).\(^{(17)}\) We calculated \(\lambda_s\) using the formula

\[
\lambda_s = \frac{\text{OR}}{1 - \text{Prev} + \text{OR(Prev)}}
\]

where “OR” is the odds of nonrecovery from chronic LBP given a co-twin with chronic LBP at baseline, and “Prev” is the prevalence of nonrecovery at follow-up in the total sample.

RESULTS

Sample Characteristics

There were 552 twins that experienced chronic LBP within the past 2 years at baseline and had available data from their...
co-twin. Of these 552 twins, 455 had data on LBP at follow-up and were included in the following analyses. A total of 183 twins (MZ = 83, DZ = 100) had an affected co-twin and 272 twins (MZ = 89, DZ = 183) did not (Table 1). The prevalence of nonrecovery was 44.2% in the total sample, 44.5% in DZ twins, and 43.6% in MZ twins. The mean age (standard deviation) of participants was 53.5 (7.0) years old, with 330 women (72.5%) and 172 MZ twins (37.8%). Twins with an affected co-twin were more likely to have poor sleep quality (64.5% vs 55.5%).

Familial Aggregation of Chronic Low Back Pain and Recovery

In our adjusted analyses, participants with a co-twin reporting chronic LBP at baseline were significantly less likely to recover from LBP at follow-up (OR = 1.6, 95% CI: 1.0–2.4, P = 0.046, n = 455; Table 2), with familial aggregation of chronic LBP significantly affecting MZ twins (OR = 2.5, 95% CI: 1.3–4.8, P = 0.006, n = 172) but not DZ twins (OR = 1.1, 95% CI: 0.6–2.0, P = 0.668, n = 283; Figure 2). The total sample analysis was adjusted for sex and sleep quality. When the analyses were stratified by zygosity, no covariables entered the multivariate models.

Sibling Recurrence Risk Ratio (λs)

Using the OR from our multivariate logistic regression models, and the prevalence of nonrecovery, we calculated λs. Having a twin (sibling) with chronic LBP at baseline appears to increase the risk of nonrecovery at follow-up (λs = 1.2), with a higher risk in MZ twins (λs = 1.5) compared to DZ twins (λs = 1.1) (Table 2).

DISCUSSION

Familial aggregation of chronic LBP increases the risk of not recovering from chronic LBP, with genetics appearing to play a role in this relationship. These results have implications for extending the understanding of factors affecting the recovery from chronic LBP beyond the individual and toward familial factors. Further research in this area has the potential to assist clinicians identify those at risk of nonrecovery.

Familial Aggregation of Chronic Low Back Pain and Recovery

A sample of twins was utilized in the present study to gain insight into the role of genetics in the recovery from chronic LBP. Our results showed that having a co-twin with chronic LBP at baseline significantly predicted nonrecovery at follow-up (OR = 1.6, 95% CI: 1.0–2.4, P = 0.046). When this analysis was, however, stratified by zygosity, the magnitude of the relationship increased for MZ twins (OR = 2.5, 95% CI: 1.3–4.8, P = 0.006) and decreased for DZ twins (OR = 1.1, 95% CI: 0.6–2.0, P = 0.668). Because MZ twins share approximately 100% of their segregating genes, whereas DZ twins only share approximately 50%, the increase in magnitude when considering only MZ twins is

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<th>TABLE 1. Sample Characteristics of Participants With Low Back Pain at Baseline and Data on Low Back Pain at Follow-up</th>
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aIndicates current smokers.
bIndicates the engagement in no/low daily physical activity and no leisure physical activity.
cIndicates being moderately/very depressed or anxious.
dIndicating the presence of sleep disturbance (>5 on the PSQI TOT scale).

BMI indicates body mass index; DZ, dizygotic; LBP, low back pain; MZ, monozygotic; n, number of subjects.
likely reflecting the role of genetics in the recovery from chronic LBP. Furthermore, the results from our sibling recurrence relative risk analysis demonstrated the risk of non-recovery increases 1.2 times in the presence of a sibling who has suffered from chronic LBP. This risk was higher in MZ twins ($\lambda_s = 1.5$), but lower in DZ twins ($\lambda_s = 1.1$), consistent with an influence of genetics factors in the recovery from chronic LBP.

Our study did not intend to explain why familial aggregation of chronic LBP affects recovery, and although genetics appear to be playing a role, additional hypotheses deserve attention. Our results appear to be consistent with existing research highlighting the negative impact having family members suffering from chronic LBP have on the prevalence,$^8$ and risk$^9$ of chronic LBP. Therefore, one possible explanation is that negative beliefs about chronic LBP, shown to be associated with greater pain and disability,$^{18}$ may have been shared among twin pairs concordant for chronic LBP, negatively affecting recovery.$^{19}$ Twin pairs share numerous environmental factors throughout their childhood,$^{16}$ with a strong twin bond potentially influencing each other’s beliefs. Furthermore, it has been suggested that MZ twins share a stronger bond compared with DZ twins.$^{20}$ The possibility of this bond increasing the influence of each other’s beliefs and potentially explaining why familial aggregation of chronic LBP had a greater effect on MZ twins cannot be ruled out. Finally, having an adult sibling with LBP appears to have a larger effect on LBP outcomes than having parents or children with LBP.$^{21}$ Therefore, shared beliefs between adult siblings in our study might explain the strong effect familial aggregation of chronic LBP has on recovery.

**Strengths and Limitations**

Our study has numerous strengths. First, we employed strict criteria for the adjustment of confounding variables. Although it is not always necessary to adjust for confounders in prognostic cohort studies, adjusting for strong known confounders allows us to make these results more generalizable.$^{22}$ Secondly, we were able to use subjective data from co-twins to inform on the familial aggregation of chronic LBP. We believe this is more accurate than participants reporting on behalf of their family members, which has previously been employed in studies investigating familial aggregation of LBP.$^8,9,23$ Thirdly, stratifying the analyses by zygosity, while performing a sibling recurrence relative risk analysis, provided insights on the contribution of genetics, which previous studies in the field have been unable to achieve. Finally, the sample of twins used in the present study are representative of the general population from

| TABLE 2. The Effect of Familial Aggregation of Chronic Low Back Pain on Recovery and the Sibling Recurrence Relative Risk ($\lambda_s$) |
|---------------------------------|--------|--------|---------|------|
| **OR**                         | **95% CI** | **P**   | **$\lambda_s$** |
| Total sample—unadjusted        | 1.5    | 1.0–2.2 | 0.064   | 1.2  |
| (n = 455)                      |        |         |         |      |
| Total sample (n = 455)$^a$     | 1.6    | 1.0–2.4 | 0.046$^*$| 1.2  |
| DZ (n = 283)                   | 1.1    | 0.6–2.0 | 0.668   | 1.1  |
| MZ (n = 172)                   | 2.5    | 1.3–4.8 | 0.006$^*$| 1.5  |

$^a$Adjusted for sex and sleep quality. All analyses were adjusted for follow-up length unless reported as unadjusted.

CI indicates confidence interval; DZ, dizygotic; MZ, monozygotic; OR, odds ratio.

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**Figure 2.** The effect of familial aggregation of chronic LBP on recovery. CI indicates confidence interval; DZ, dizygotic; LBP, low back pain; MZ, monozygotic; OR, odds ratio.
which they were drawn and can be considered representative of the non-twin population for the prevalence of numerous diseases, including LBP.24 Our study, however, presented a few limitations which need to be considered. First, our assessment of chronic LBP at baseline was based on the following question: “Have you experienced chronic LBP in the last 2 years?” As a result, participants at baseline did not necessarily experience chronic LBP at study entry. Second, our outcome variable for the recovery from chronic LBP gives us an indication of whether the participant experienced LBP within the past 4 weeks, but does not give us information on LBP disability or pain intensity. Because these data were not collected from participants specifically for this episode of LBP, we were unable to investigate whether familial aggregation of chronic LBP affects disability or pain intensity at follow-up. In addition, baseline data on care seeking and treatment would have been valuable to determine whether the effect familial aggregation of chronic LBP has on recovery is moderated by ongoing treatment. Third, we did not have adequate data on LBP from the 2007 collection wave, and did not have data on LBP between assessment points. This information would have been valuable for analyzing the recurrence or persistence of LBP symptoms over time. Finally, our definition of familial aggregation of chronic LBP only considered data from the co-twin, without considering characteristics of the whole family. This would, however, likely underestimate the true effect of familial aggregation, because both twins with, or without a co-twin with chronic LBP may have had other family members with chronic LBP.

Clinical Implications

Obtaining information from patients regarding family history of chronic LBP has the potential to inform which patients are less likely to recover, and help clinicians make more accurate prognosis. More importantly, an understanding of the mechanisms behind familial aggregation of chronic LBP and nonrecovery (such as the relative contribution of genetics and environmental factors to LBP) may have the potential to inform the direction of treatment. For example, if negative beliefs about LBP have been passed on by family members with chronic LBP and are significantly affecting recovery, providing the appropriate reassurance and education could be extremely valuable. In addition, the plausibly important role of genetics on the prognosis of chronic LBP should lead to attempts to identify genetic variants for these phenotypes. Therefore, further studies on quantitative and molecular genetics (e.g., genome-wide association studies) should investigate the pathways between familial aggregation of chronic LBP and nonrecovery to build on these results.

CONCLUSION

Familial aggregation of chronic LBP significantly predicted nonrecovery, with genetics playing a role in this relationship. Although previous research has considered familial factors associated with LBP, the present study is the first to investigate how familial aggregation affects recovery. Future research should further explore familial aggregation in the recovery from LBP, and investigate the mechanisms behind familial predictors of nonrecovery.

Key Points

- Familial aggregation of chronic LBP increases the risk of not recovering from chronic LBP.
- Genetics appear to play a role in the recovery from chronic LBP, with familial aggregation of chronic LBP having a larger effect on nonrecovery in identical twins than in fraternal twins.
- The presence of chronic LBP within a family has the potential to inform clinicians on which patients are less likely to recover and may guide future management strategies.

Acknowledgments

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References


