Previous Injury and Chronic Pain are Associated with Side of Onset in Parkinson's Disease

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Abstract

Background

Parkinson’s disease (PD) motor symptoms are frequently asymmetric and the factors that influence the side of onset are unclear.

Objective

To explore whether peripheral injury and associated chronic limb pain may influence the side of onset.

Methods

We administered a questionnaire to 128 PD patients in a tertiary movement disorder clinic. Handedness, date and type of limb injury(s) and duration of associated pain, and date and side of onset were ascertained.

Results

Sixty-two subjects reported limb injuries prior to the onset of PD symptoms, 30 with and 32 without chronic pain (i.e., ≥ 2 months). There was no association between injury and PD onset side overall (p=0.334). In subjects with chronic pain associated with limb injuries, however, side of injuries was associated with the side of PD symptom onset (p=0.030).

Conclusions

Limb injury with chronic pain may be related to the side of PD symptom onset. Future studies may shed light on the nature of this observation.

Keywords: Parkinson’s disease; Peripheral limb injury; Side of onset; Handedness

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multiple limb injuries in their lifetime, we developed a system to assess the dominant side of past limb injuries. First, we generated a scoring system to gauge the intensity and duration of pain associated with each injury (Supplementary Table 2). Then, we obtained a composite score of each injury by multiplying the intensity score with the duration score. The dominant injury side was defined as the side with the highest combined score.

We compared demographic and clinical characteristics for the groups by t-test, chi-square test, and Fisher’s exact test, as appropriate. The effects of injury and handedness on side of PD onset were evaluated by Fisher’s exact tests. The Cochran-Mantel-Haenszel test was used to assess the association between injury and side of PD onset. A two-sided p value of <0.05 was considered statistically significant.

Results

Of the 128 PD subjects, 126 PD subjects were able to answer the limb injury questionnaire. Among them, 62 (49%) subjects experienced injury(s) versus 55 of 116 controls (47%; p=0.780). Among the 128 PD subjects, 114 PD subjects had known history of injuries and clear asymmetrical side of onset, and were included in the analysis for the effect of injury on PD onset side.

The side of injury had no significant influence on the side of onset in subjects with both acute and chronic injuries (p=0.334, Figure 1, top). There was, however, a significant influence of side with chronic pain on PD side of onset, with concordant rates of 64% and 73% for right and left side injury and onset, respectively, (p=0.030, Figure 1, bottom). After adjusting for handedness, the trend persisted (p=0.067).

Discussion

The factors underlying the asymmetric presentation of PD have puzzled the field. This study explored for the first time the potential relationship between limb injury and PD side of onset. The results do not support the notion that limb injury is associated with PD side of onset; however, chronic pain associated with injury may be linked to the side of PD onset. The latter observation is both novel and intriguing, although the exact nature of the association is unknown.

In the past, animal experiments have shown that peripheral limb injury can modulate brain function [4,7]. Animals subjected to thermal injury have been shown to have reduced movement of the affected limb, and decreased enkephalin content of the globus pallidus, especially after prolonged duration [4]. In addition, peripheral injury also has been implicated in dystonia [4,5,8]. Thus, it is possible that peripheral limb injury may modulate the BG and influence the side of symptom onset of PD. On the other hand, it is well known that PD can affect many non-motor systems. Chronic pain has been known to be part of PD, as many PD patients have reported differential pain [9], and levodopa has been shown to be associated with increased pain threshold in PD [10]. Thus, it is conceivable that higher chronic pain from limb injuries may represent the lower pain threshold in the pre-PD state.

This study is limited by being relatively small scale, retrospective, and the arbitrary categorization of injuries. In addition, we did not account for other conditions associated with chronic limb pain. Nevertheless, this is the first exploration of whether there is a link between chronic pain associated with past limb injury and side of PD onset. The results warrant future studies, and may have important clinical and basic scientific implications.

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Disclosure of Conflicts of Interest

None of the authors have any to disclose.

References


