The Effect of Comorbid Allergies on the Physical and Psychosocial Outcomes of MS patients – a Th1/Th2 paradigm of Autoimmune Disease

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Background
Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease of the Central Nervous System (CNS). It is an autoimmune disorder primarily characterized by an abnormal response of CD4+ T helper (Th1) cells against myelin self-antigen while allergies and asthma are the result of an abnormal response of the Th2 cell lineage and its respective cytokines (Figure 1). The beneficial therapeutic effect of several of the approved MS therapies are linked to their ability to switch from a Th1 to a Th2 milieu.

Demographic Results
There was no significant difference between the two groups in sex, race, smoking status, or DMFT use. However, there was an association between allergies and education status (those with allergies were more likely to have at least a college education; 74.3% vs 66.4% in the group without allergies; p<0.001). At enrollment, the allergy group had a higher proportion of Relapsing Remitting MS (RRMS) (72.2% vs 65.6%; p=0.001) compared to subjects not reporting allergic symptoms, despite having the same disease duration (mean 10.2 [SD=9.6] vs 10.3 [SD=9.7], respectively). This difference persisted at 5 years but was no longer statistically significant (p=0.07).

Psychosocial Results – Enrollment & 5-year-follow-up
At enrollment, participants with allergies reported more anxiety (38.5% vs 33.6%, p=0.071), guilt (77.7% vs 80.6%, p=0.036), loneliness (38.9% vs 39.8%, p=0.001), and loneliness (17.8% vs 15.2%, p=0.012), and were more likely to report pain (53.8% vs 47.2% p=0.01) compared to the group without allergies. However, at 5 year follow up, all differences in the perception of negative feelings between the groups disappeared. There was no difference in perceived pain (56.5% in the allergy group vs 48.2% in the group without, p=0.003).

Objective Physical Limitation at Enrollment

Discussion
We found an association between reporting comorbid allergies and more psychological impairment at enrollment and, with a loss of significance, at follow up. For physical impairment, the allergy group had marginally better EDSS scores and T25FW times at enrollment and follow up, but EDSS differences were only statistically significant at enrollment, and T25FW differences were only statistically significant at 5 year follow up. This is mostly in agreement with a previous survey study that showed an association between allergies and psychological impairment in MS but not with physical disability. We anticipate that the loss of significance may be attributed to some limitations of our study including a large loss-to-follow-up at the 5 year mark (Allergies: 2,548 to 623; No allergies: 2,548 to 687) which decreased the power of the study; and a reliance on self-reported diagnosis of allergies. However, our study also has several strengths, including: the use of a large well-established cohort of MS patients with routine clinical follow up, our ability to match the allergies and non-allergies group on several possible confounding demographic variables, and the extensive data about physical and psychosocial limitations that we had.

Physical Results – Enrollment & 5-year-follow-up
At enrollment, the allergy group had lower mean EDSS scores (3.3 [SD=2.2] vs 3.6 [SD=2.2], p=0.07) and T25FW difference in mean T25FW times (8.3 [SD 10.3] vs 8.6 [SD 10.9] seconds, p=0.293). At 5 year follow up, the difference in EDSS scores persisted (4.0 [SD 2.4] vs 4.2 [SD 2.4], p=0.17) but was not significant. T25FW times became statistically significant at 5 year follow up with the allergy group averaging 8.7 [SD 10.2] vs 10.6 [SD 14.6] seconds, p<0.001.

Methods
We conducted a retrospective matched case-control study comparing MS patients with and without allergies using 5,966 subjects extracted from the New York State MS Consortium. The presence of allergies was determined through a self-reported questionnaire at study enrollment. The groups were matched 1:1 on sex, age, and disease severity. Chi-square tests and independent samples t-tests were used to analyze differences in measures between the two groups. A subsample of 1,310 subjects was analyzed to investigate group differences at 5 years after study enrollment.

References
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Objective Physical Limitation at Follow-up

Figure 1: Naive CD4 (Th0) cell differentiating into Th1 and Th2 cells.

Figure 2A: Graph of participants’ perceived psychosocial impairment at enrollment by whether they had comorbid allergies.

Figure 3A: Graph comparing EDSS score and T25FW times at enrollment.

Figure 3B: Graph comparing EDSS score and T25FW times at follow-up.

Figure 3C: Graph of participants’ perceived psychosocial impairment at follow-up by whether they had comorbid allergies.

Psychosocial Results – Enrollment & 5-year-follow-up

Discussion
We found an association between reporting comorbid allergies and more psychological impairment at enrollment and, with a loss of significance, at follow up. For physical impairment, the allergy group had marginally better EDSS scores and T25FW times at enrollment and follow up, but EDSS differences were only statistically significant at enrollment, and T25FW differences were only statistically significant at 5 year follow up. This is mostly in agreement with a previous survey study that showed an association between allergies and psychological impairment in MS but not with physical disability. We anticipate that the loss of significance may be attributed to some limitations of our study including a large loss-to-follow-up at the 5 year mark (Allergies: 2,548 to 623; No allergies: 2,548 to 687) which decreased the power of the study; and a reliance on self-reported diagnosis of allergies. However, our study also has several strengths, including: the use of a large well-established cohort of MS patients with routine clinical follow up, our ability to match the allergies and non-allergies group on several possible confounding demographic variables, and the extensive data about physical and psychosocial limitations that we had.

Of note, the increased association between comorbid allergies and having RRMS supports a current hypothesis that having a history of atopic allergy reduces the risk of both development and progressive MS. The pathogenesis remains unclear, however, there is data to suggest that during the relapsing stage a pro-inflammatory response that involves both the adaptive and innate immune system dominates while during the progressive stage abnormalities of the innate immune system prevail. Patients with allergies may have Th2 cells that behave in a regulatory manner to redirect the immune system away from an innate response thus delaying the onset of progressive stage of MS.

Conclusion
In conclusion, we observed a small but significant association between reporting comorbid allergies and a higher number of RRMS after 10 years and a trend after 15 years of disease duration. Lower EDSS scores and a stronger association with psychosocial impairment at enrollment. More studies are required to explore the role of Th2 co-morbid disorders associated with MS for more individualized appropriate therapies.

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