Exposure to *Juniperus ashei* (Mountain Cedar) and *Quercus virginiana (*Virginia Live Oak) Pollen Exhibit Different Levels of Concordance in Symptoms in a Pollen Challenge Chamber vs. Natural Season   Abstract #177

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Abstract

Rationale: The level of concordance between allergic symptoms induced upon exposure to pollen in a pollen challenge chamber (PCC) versus the natural season, and if the concordance is dependent on the allergen, has not been well studied.

Methods: Seventeen Mt. Cedar-positive subjects (MCPS) and 7 Mt. Cedar-negative (MCNS) were challenged to Mt. Cedar pollen in a PCC for 3 hours per day for 2 days as well as recorded symptoms for 30 days during the natural Mt. Cedar season. A similar study was conducted using Virginia Live Oak (VLO) pollen for 24 VLO-positive (VLOPS) and 14 VLO-negative subjects (VLONS) in the PCC for 3 hours per day for 2 days and recorded symptoms for 51 days during the natural VLO season.

Results: When looking at all subjects, the correlation between the maximum total symptom scores (max TSS) recorded in the natural season and PCC was very high (Mt. Cedar r = 0.82, P < 0.001; and VLO r = 0.78, P < 0.001). When restricted to positive subjects, the max TSS in MCPS still remains high (r = 0.66; P = 0.004), but the correlation in VLOPS significantly decreases (r = 0.38; P = 0.069). When looking at all subjects, three Mt. Cedar subjects (12.5%) and five VLO subjects (13.2%) had discordant max TSS in the PCC when compared to the natural season.

Conclusions: Our findings suggest that a two day PCC run mimics the natural season when Mt. Cedar pollen is used, but not when VLO pollen is used. This study shows the utility of the PCC as a model to explore mechanisms underpinning allergic rhinoconjunctivitis as well as for evaluating efficacy of therapeutic agents, but also illustrates the importance of allergen selection.

Introduction

Allergic rhinoconjunctivitis (AR) is an extremely common illness, affecting nearly 20% of the population. While not life threatening, allergic rhinitis can lead to complications that can significantly impair one's quality of life[1], and this in turn leads to several indirect costs. It is estimated that the total direct and indirect costs due to allergic rhinitis each year is $5.3 billion[2] and that a person who suffers from AR has, on average, $1,500 in incremental healthcare costs in a single year[3]. Pollen challenge chambers (PCC) have been utilized for many years to study certain characteristics of drugs by stimulating symptoms in controlled environments in order to avoid the effect of ill-defined co-factors. A previous study showed that a PCC could be used to adequately mimic the ragweed natural season[4], without the confounders that might be present during the natural season. This study examined whether symptoms elicited following challenge to Mt. Cedar and Virginia Live Oak (VLO) in a PCC are similar to those elicited in a natural season.

Methods

Data Collection
- Seventeen Mt. Cedar positive subjects (MCPS), seven Mt. Cedar negative subjects (MCNS), twenty-four VLO positive subjects (VLOPS), and fourteen VLO negative subjects (VLONS) meeting entry criteria, were exposed to Mt. Cedar and VLO pollen respectively during 2 PCC runs of 3 hours duration on consecutive days and were also followed in their respective natural season.
- Total symptom score (TSS) was recorded every 30 minutes during the PCC runs.
- TSS was recorded every morning and evening during the natural season; the average of each day was calculated.
- **Figure 1** shows entry criteria and study design.

Statistical Analysis
- Maximum (max) TSS was calculated as follows: for each individual, their mean TSS as well as the standard deviation of the mean TSS was calculated, and the max TSS was the maximum observed TSS that was within two standard deviations of the mean TSS.
- To determine concordance, the standard deviation (SD) of the difference between max TSS in the natural season and PCC was calculated. Any subject whose max TSS in PCC was within 2 SD of the natural season was called concordant.
- Pearson correlation coefficients were used to compare max TSS recorded in the natural season and PCC.
- Linear regression was used to determine if the association between max TSS in the natural season and in the PCC differed based on allergen.
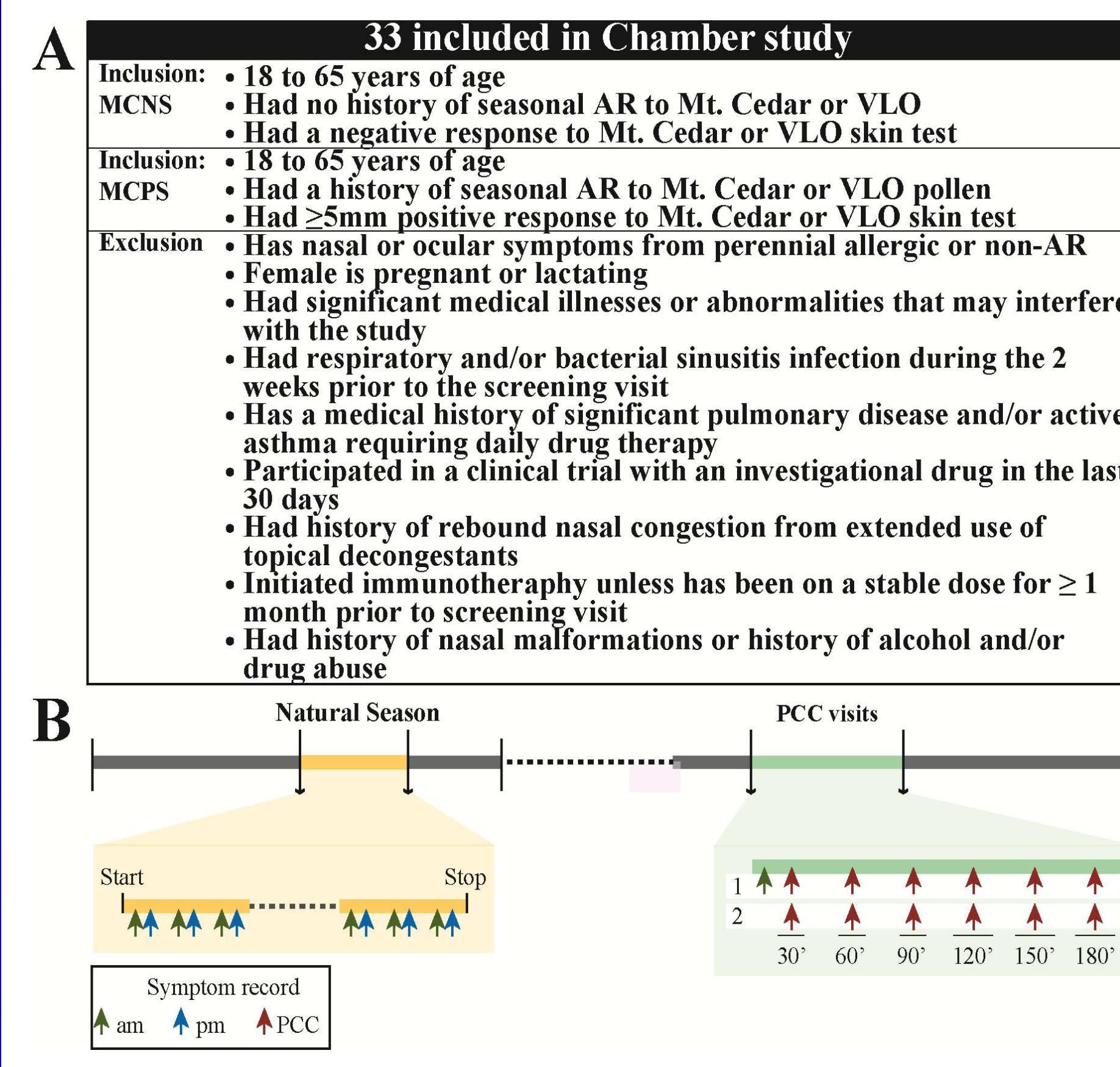

Figure 1: Inclusion/exclusion criteria and study design. A) Shows the inclusion criteria for MCNS and MCPS and the exclusion criteria. **B)** Flow diagram showing the study design.
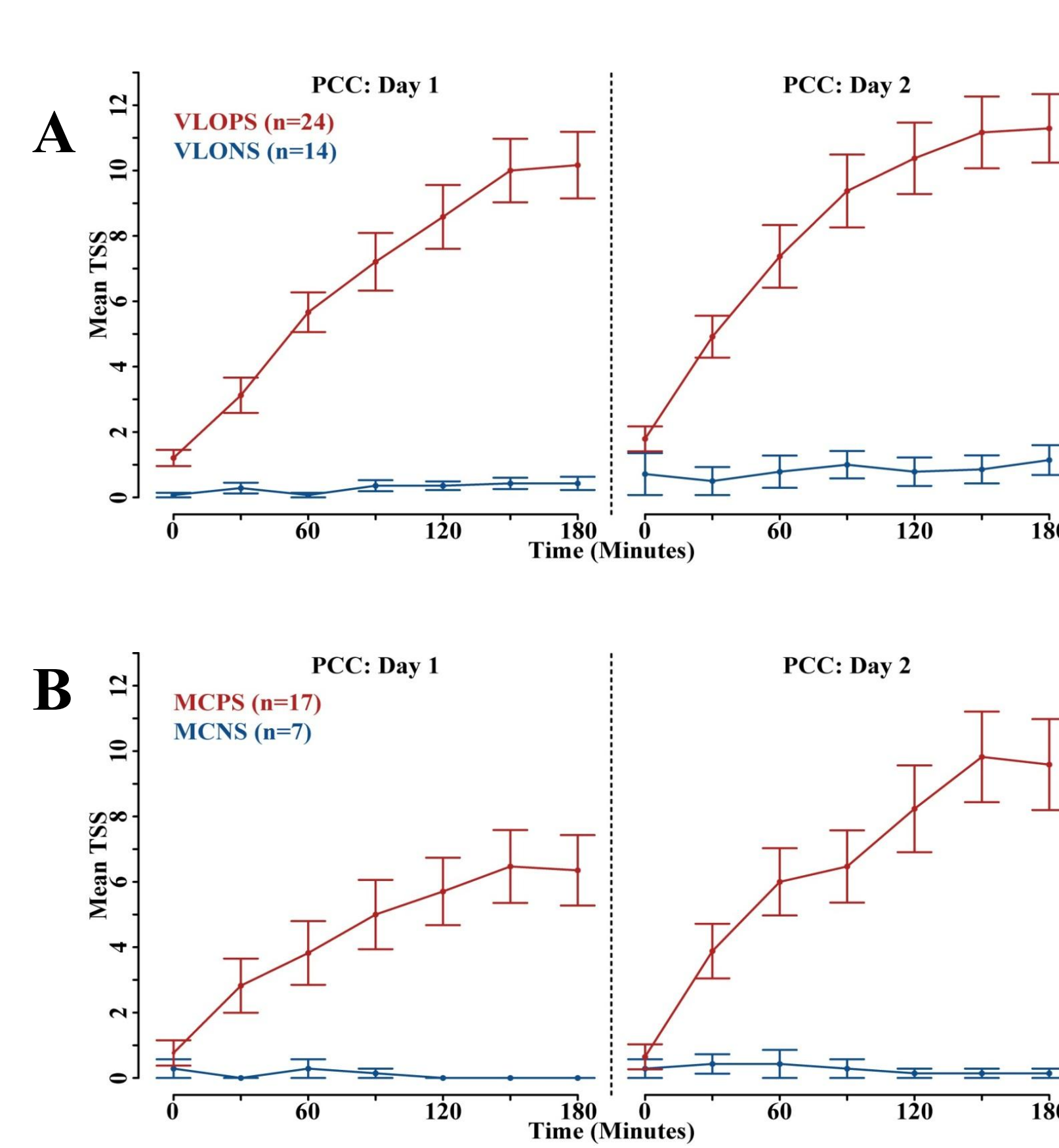

Figure 2: Total Symptom Score (TSS) A) Mean TSS with standard error bars at thirty minute intervals on day 1 and day 2 of the PPC run for VLO. **B)** Mean TSS with standard error bars at thirty minute intervals on day 1 and day 2 of the PPC run for Mt. Cedar
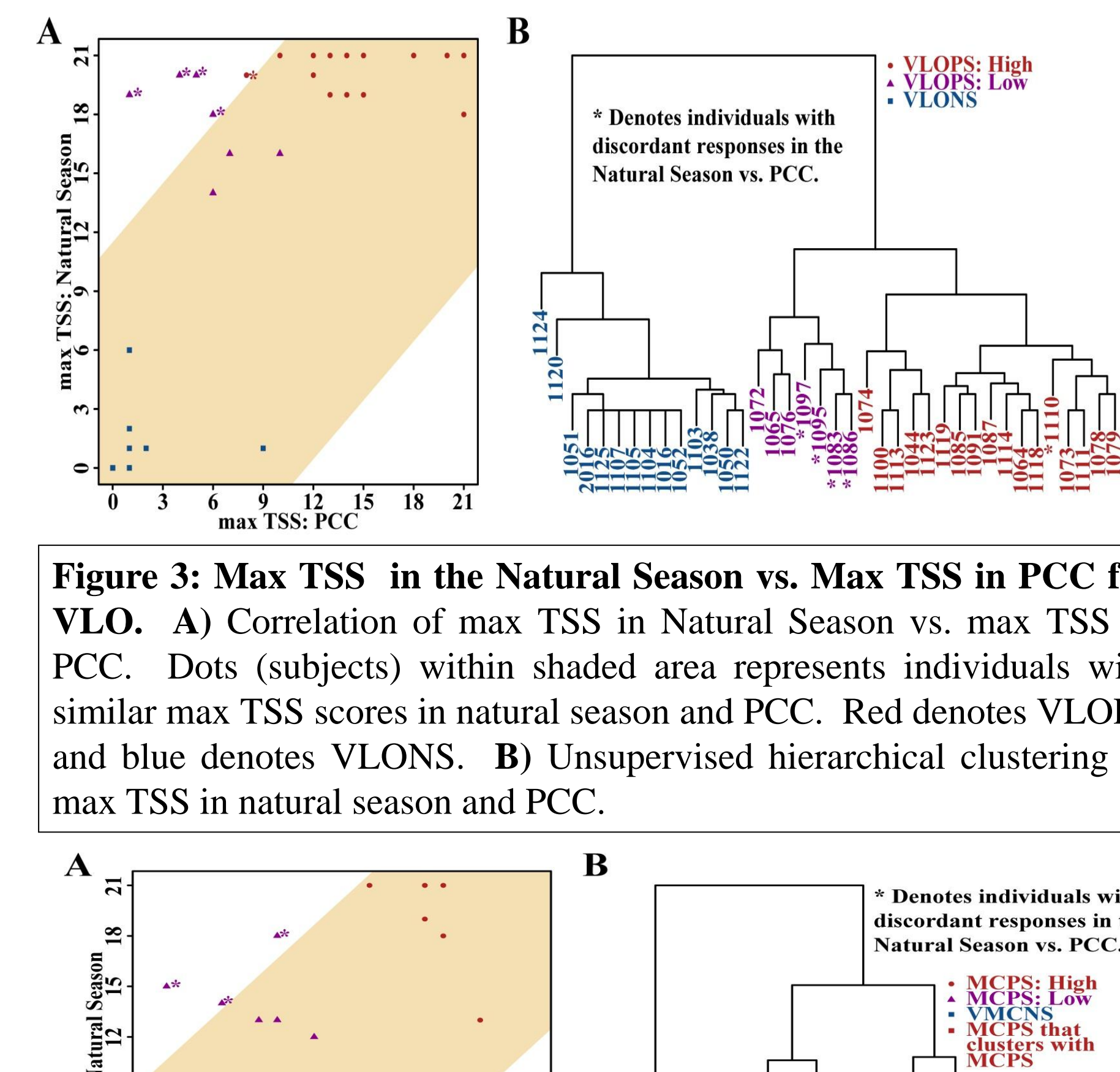

Figure 3: Max TSS in the Natural Season vs. Max TSS in PCC for VLO. A) Correlation of max TSS in Natural Season vs. max TSS in PCC. Dots (subjects) within shaded area represents individuals with similar max TSS scores in natural season and PCC. Red denotes VLOPS and blue denotes VLONS. **B)** Unsupervised hierarchical clustering of max TSS in natural season and PCC.
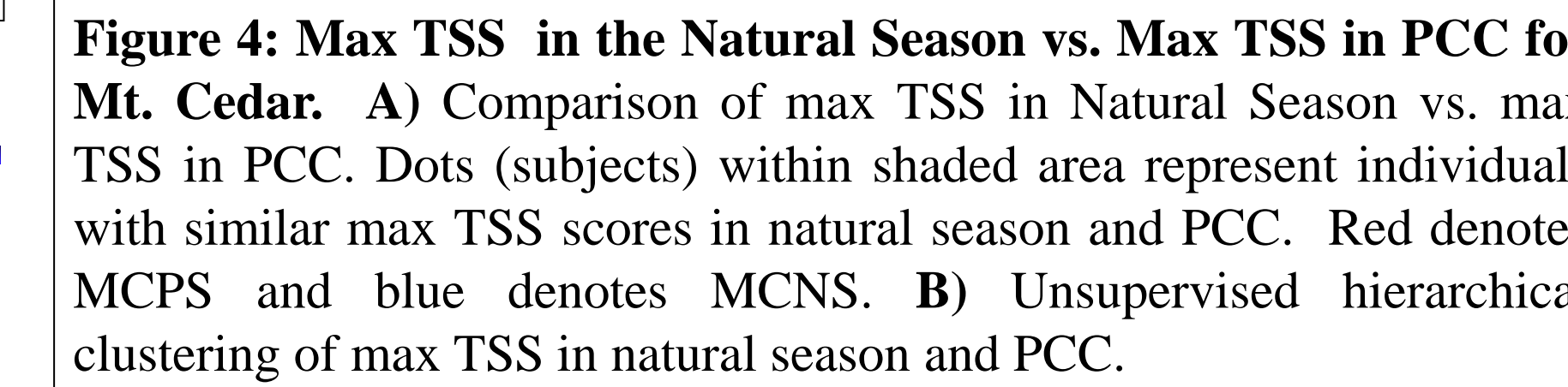
Figure 4: Max TSS in the Natural Season vs. Max TSS in PCC for Mt. Cedar. A) Comparison of max TSS in Natural Season vs. max TSS in PCC. Dots (subjects) within shaded area represent individuals with similar max TSS scores in natural season and PCC. Red denotes MCPS and blue denotes MCNS. **B)** Unsupervised hierarchical clustering of max TSS in natural season and PCC.
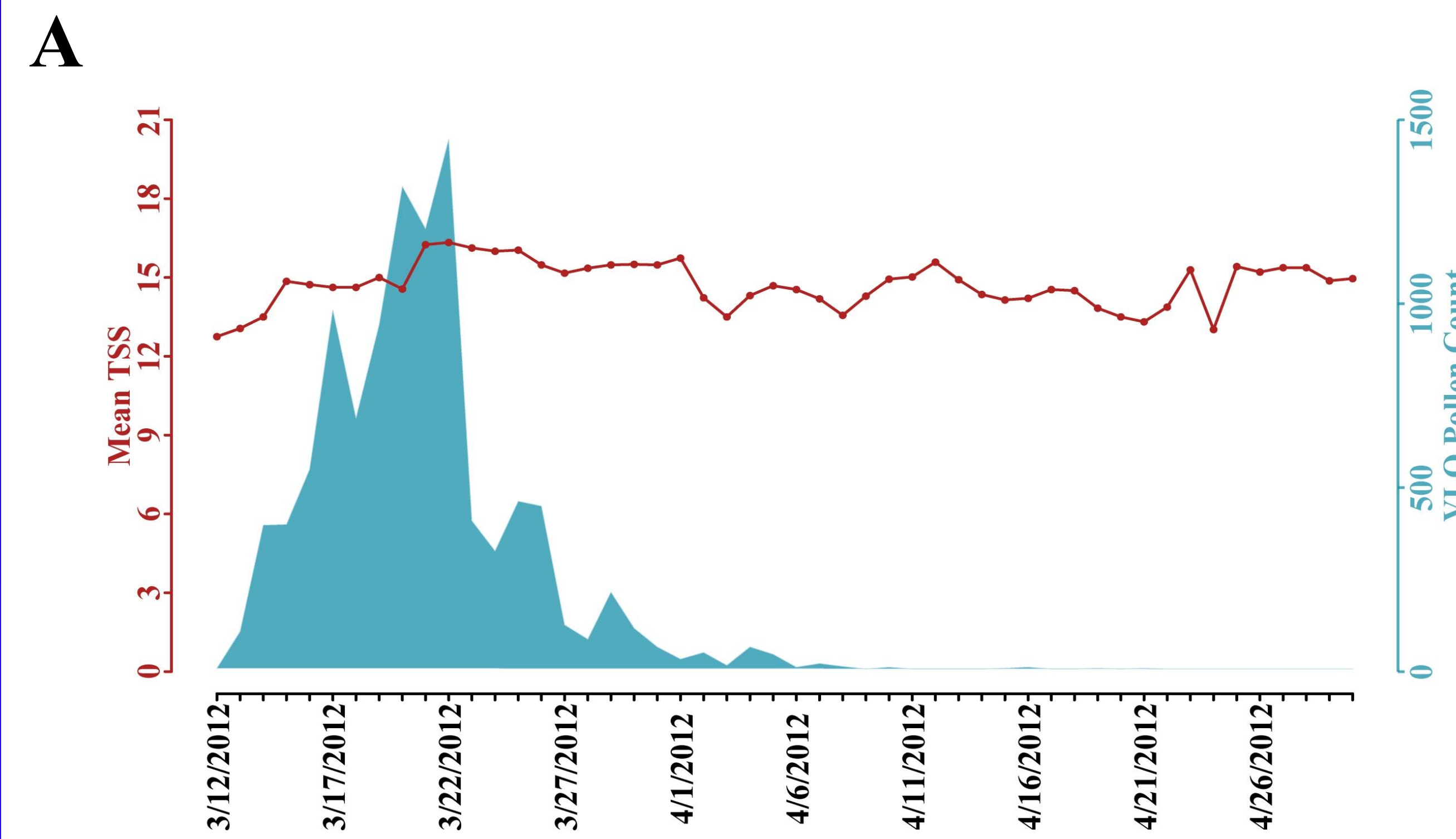
Figure 5A: Mean TSS for VLOPS (red dots) in the Natural Season along with VLO pollen count (blue shade).
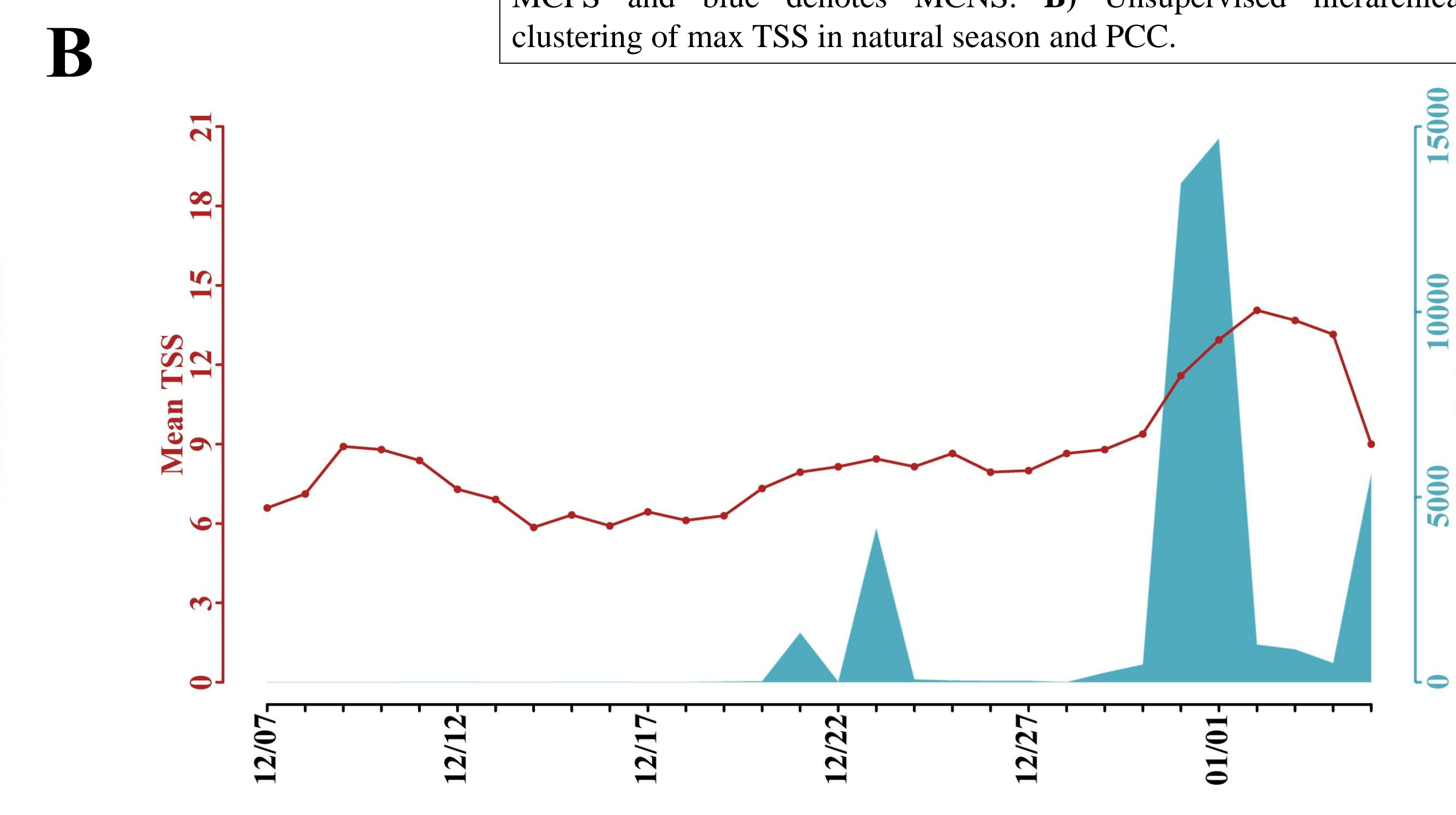
Figure 5B: Mean TSS for MCPS (red dots) in the Natural Season along with MT Cedar pollen count (blue shade).

Results and Discussion

Figure 2 shows that compared with non-atopic subjects, individuals with allergies to Mt. Cedar or VLO develop symptoms following exposure to pollen in the PCC; TSS is higher following the second PCC run, especially in MCPS subjects. Correlation between the max TSS in the natural season vs. max TSS in the PCC is shown in **figure 3A** for VLO subjects and **figure 4A** for Mt. Cedar subjects. When atopic and non-atopic subjects are examined as a group, there is a strong correlation between the max TSS recorded in the natural season and in the PCC for both VLO and Mt. Cedar (r = 0.78; P < 0.001 and r = 0.82; P < 0.001, respectively). **Figure 3B** and **figure 4B** depicts the unsupervised hierarchical clustering of participants exposed to VLO and Mt. Cedar, respectively, and demonstrates that Mt. Cedar or VLO atopic subjects form a cluster distinct from non-atopic subjects.

However, Mt. Cedar atopic subjects further categorize into those who have high vs. low TSS scores in both the PCC and natural season (**figure 4B**). In contrast, while VLO atopic subjects also formed two clusters, one cluster comprised individuals who had low TSS in the PCC but high TSS in the natural season, whereas the second comprised individuals with high TSS in both the PCC and the natural season (**figure 3B**). Thus, MCPS have a higher level of correlation of max TSS recorded in the natural season and the PCC (r = 0.66; P = 0.004) while the correlation is lower in the VLOPS (r = 0.38; P = 0.069). There was a significantly higher association between the max TSS recorded in the natural season and PCC among MCPS compared with VLOPS (P = 0.006).

There is a likely reason for the lower correlation between the max TSS in the natural season vs. the PCC among VLOPS compared with MCPS. **Figure 5** shows the mean TSS and pollen count during the natural season for VLO (**panel A**) and Mt. Cedar (**panel B**). In the natural VLO season, VLO atopic subjects entered the season with high TSS (mean = 12) and then coincident with the spike in VLO counts in the environment VLOPS experienced a modest increase (25%) in mean TSS (**figure 5A**). In contrast, in the natural Mt. Cedar season, Mt. Cedar atopic subjects entered the season with lower TSS (mean = 6) than those observed for the VLO atopic subjects, and coincident with the spike in Mt. Cedar counts in the environment, MCPS experienced a more brisk increase (approximately 200%) in mean TSS (**figure 5B**).

Conclusion

This study demonstrates that a PCC can be used as an effectively model AR without the confounding of elevations in symptom scores prior to entering the natural season. These elevated symptom scores may be related to responses to antigens other than VLO or Mt. Cedar pollen. Thus we suggest that the PCC is an ideal approach to evaluated mechanisms underpinning allergic rhinoconjunctivitis as well as efficacy of therapeutic agents as it can accurately mimic the natural season while eliminating possible confounders.

References

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