Abstract Form

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Project Title:	A Novel Methodology to Visualize Evolutionary Trade-Offs Underlying Vulnerability to the Development of POTS

Research Category (please check one):

☐	**Original Research**	☐	**Clinical Vignette**	☐	**Quality Improvement**	☒	**Medical Education Innovation**

Abstract

Introduction:
Postural orthostatic tachycardia syndrome (POTS) is an autonomic disorder characterized by inadequate maintenance of blood pressure related to postural changes. POTS has a prevalence of 0.2% in the general public and is seen in females more than males. Vulnerability to POTS may represent an evolutionary byproduct of selection for critical biological functions, most likely related to autonomic function. Identifying the critical pathways under selection can strengthen our understanding of the pathophysiology and clinical course of POTS.

Methods:
A gene set was curated for POTS using LifeMap Sciences' MalaCards, followed by a gene enrichment analysis through Gene Ontology, a publicly available bioinformatics platform that determines which biological pathways contain the inputted POTS genes. A novel scoring system developed for this project, the Smolens-Mazmanian Index (SMI), was used to highlight the biological processes most likely underlying vulnerability to POTS. Application of SMI allows for the results of Gene Ontology to be ranked by the greatest percent of overlapping genes between POTS and each biological process. After establishing the top 10 SMI-ranked biological processes, gene sets were respectively compiled for each. The R package Tidyr was used to create a presence-absence matrix for the genes in each biological process that are present in the POTS gene set. An interactive visualization was designed using the publicly available platform Flourish to illustrate the biological process's genes that most overlap with POTS pathology.

Results:
Analysis and visualization of the findings reveal a number of specific pathways under selection. The top 3 pathways that each had an SMI score of 133.33 were negative regulation of endodermal cell differentiation, norepinephrine-epinephrine-mediated vasodilation involved in regulation of systemic arterial blood pressure, and renin-angiotensin regulation of aldosterone production. The next two pathways were regulation of blood volume by renin-angiotensin with a score of 112.5, followed by sequestering of TGFbeta in extracellular matrix with a score of 100.

Conclusion:
Application of SMI can be used to accelerate biomedical innovation leading to more effective therapeutic interventions for POTS. Identification of the biological pathways activated in the setting of POTS holds promise to clarify the factors triggering and sustaining this condition. Moreover, the application of this evolutionary perspective opens the door to a deeper understanding of this clinically debilitating disorder.