

Postural Orthostatic Tachycardia Syndrome (POTS) in Adolescents and Young Adults with CHARGE Syndrome

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Background

- CHARGE syndrome (CS) is a rare and complicated multi-system condition
- Cases of experiences with dysautonomic symptoms came to the attention of researchers.
- POTS results from autonomic dysregulation, characterized by increased heart rate on standing and return to normal when lying down
- POTS affects approximately 1% of the general population
- A case report confirmed POTS in a 17-year-old female with CS, prompting further investigation

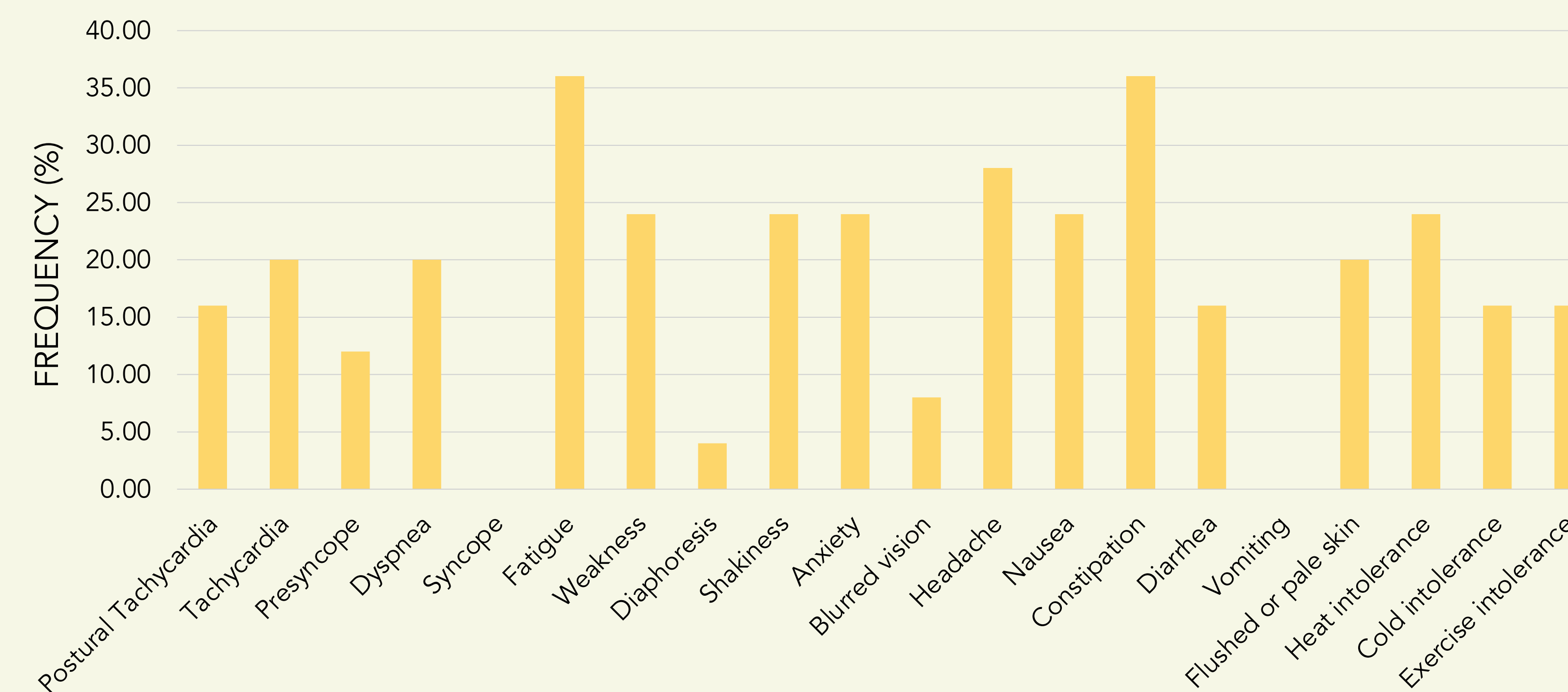
Methods & Results

- Qualitative and quantitative data were collected
- Quantitative data was collected in the form of a questionnaire designed by the research team, modelled after the COMPASS 31
 - 20 symptoms were included
 - Symptoms were measured on a 5-point Likert scale: 1 as never, 2 as occasionally (once or twice per year), 3 as sometimes (happens monthly) and 4 as often (happens weekly)
- Individuals and parents of individuals with CS were encouraged to share personal stories and experiences as part of our qualitative data collection

- 25 individuals completed the POTS component of the questionnaire
- Symptoms reported "weekly" are shown in Table 1

Results

Table 1. Symptoms experienced on a weekly basis



- Data was separated based on symptom frequency: it was noted that individuals who experienced a larger number of symptoms were also reporting these as happening with a higher frequency (and vice versa)
- The overall average number of symptoms reported on a weekly basis was 3.72 – participants were stratified based on whether they experienced 4 or more symptoms weekly (Group A, n=10), or whether they experienced 3 or fewer symptoms (Group B, n=15)

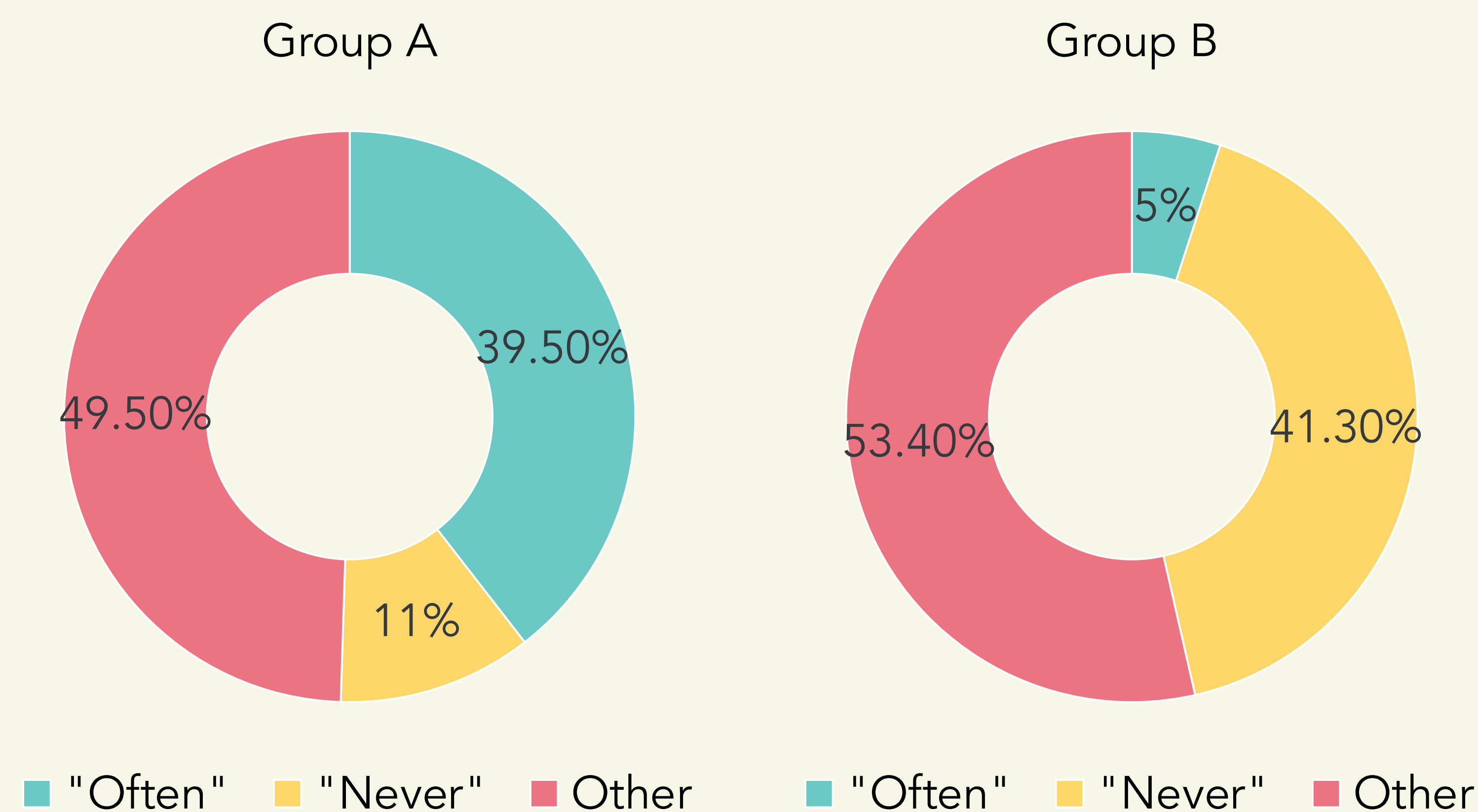


Figure 1. Average percentage of participants in each group who experienced symptoms "often" (weekly) vs. "never."

Qualitative Themes

headache chest pain
 emergency surgery fatigue sweaty
 dizzy POTS heart test
 missing school hot weather
 grand mal seizure

Discussion & Conclusions

- Nearly 40% of individuals with CS may also meet diagnostic criteria for POTS (compared to 1% of the general population)
- Qualitative data highlighted some important themes: severity of POTS or POTS-like symptoms, experience of frustration regarding lack of diagnosis or information about how to manage these symptoms
- Early detection of POTS in this population has the potential to avoid distress associated with these episodes and improve the individual's quality of life. It is important that clinicians be aware of the possibility of an individual with CHARGE syndrome presenting with symptoms of POTS and refer for testing when appropriate

References:

Bagal, R., Chan, D. A., Rada-Salas, A., Zhang, J., Xiong, Y., Hains, J., Chang, C. P., Zhao, Y., Saigal, T., & Wysocka, J. (2019). CHD3 cooperates with BRG1 to control multiplexed Neural Crest Formation. *Nature*, 469(7453), 956-962. <https://doi.org/10.1038/s41586-019-1073-3>

Berggren, K., Sjarns, B., Gennarelli, J., & Gennarelli, J. C. (2014). Postural orthostatic tachycardia syndrome, neurally mediated syncope, and joint hypermobility: A case report. *Neurologia (English Edition)*, 29(7), 447-449. <https://doi.org/10.1016/j.neuro.2014.01.006>

Blake, K. D., Herberich, T. S., Lawand, C., Dator, A. N., & Thelin, J. W. (2008). Cerebral nerve manifestations in charge syndrome. *American Journal of Medical Genetics Part A*, 144(4), 985-992. <https://doi.org/10.1002/ajmg.a.32179>

Blake, K. D., Davignon, S. L., Hall, D., Heller, M. A., Pagon, R. A., Williams, M. S., Lin, A. E., & Gahl, J. M. (1998). Charge association: An update and review for the primary pediatrician. *Clinical Pediatrics*, 37(3), 159-173. <https://doi.org/10.1177/00099228980370302>

Blake, K. D., & Prasad, C. (2004). Charge syndrome. *Orphanet Journal of Rare Diseases*, 1(1). <https://doi.org/10.1186/1750-1172-1-38>

Blake, J. R. (2018). Postural orthostatic tachycardia syndrome in children and adolescents. *Autonomic Neuroscience*, 215, 97-101. <https://doi.org/10.1016/j.autneu.2018.05.004>

Chen, Y., Steeds, S. L., Steeds, M. K., Cole, R. P., Smith, F. M., Pylkko, S. V., Brown, M. M., Midgen, C., Blake, K., & Berman, J. N. (2018). Etiology and functional validation of gastrointestinal motility dysfunction in a zebrafish model of charge syndrome. *The FASEB Journal*, 32(11), 2152-2160. <https://doi.org/10.1096/fj.201804013>

Galland, E. M., Castellano, J. E., & Raj, S. (2015). Postural tachycardia syndrome: Beyond orthostatic intolerance. *Current Neurology and Neuroscience Reports*, 15(9). <https://doi.org/10.1007/s11910-015-0543-8>

Grubb, B. P. (2008). Postural Tachycardia Syndrome. *Circulation*, 117(21), 2814-2817. <https://doi.org/10.1161/CIRCULATIONAHA.107.141611>

Hartstock, M. E., Guethala, N. E., Fink, N., Samson, R. A., Kewer, S. E., & Berber, B. J. (2008). Postural orthostatic tachycardia in teenagers with Klippel-Traneer syndrome. *Congenital Heart Disease*, 3(4), 400-402. <https://doi.org/10.1111/j.1747-0803.2008.00278.x>

Herberich, T. S., Radu, A., MacCusker, J., Karmali, B., Nakamoto, T., Harthorn, T., & Blake, K. (2014). Quality of life in adolescents and adults with charge syndrome. *American Journal of Medical Genetics Part A*, 158(8), 2012-2021. <https://doi.org/10.1002/ajmg.a.32719>

Pagon, R. A., Gahl, J. M., Zeman, J., & Yong, S. L. (1981). Coloboma, congenital heart disease, and CHARGE syndrome with multiple anomalies: Charge association. *The Journal of Pediatrics*, 99(2), 223-227. [https://doi.org/10.1016/0022-3476\(81\)90454-4](https://doi.org/10.1016/0022-3476(81)90454-4)

Paul, S., Rajag, R., & Borhen, A. (2017). Charged with neural crest defects. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*, 173(6), 478-486. <https://doi.org/10.1002/ajmg.c.31588>

Raj, S. (2004). The Postural Tachycardia Syndrome (POTS): pathophysiology, diagnosis & management. *Indian pacing and electrophysiology journal*, 42(2), 84-90. <https://doi.org/10.1177/0099228903042002>

U.S. Department of Health and Human Services. (2017). Postural orthostatic tachycardia syndrome. Genetic and Rare Diseases Information Center. Retrieved May 3, 2021, from <https://rarediseases.info.nih.gov/diseases/291/charge-syndrome>

U.S. Department of Health and Human Services. (2017). Postural orthostatic tachycardia syndrome. Genetic and Rare Diseases Information Center. Retrieved February 4, 2021, from <https://rarediseases.info.nih.gov/diseases/291/postural-orthostatic-tachycardia-syndrome>

Vissers, L. E., van Ravenswaay, C. M., Admiraal, R., Hurst, J. A., de Vries, B. B., Jansen, I. M., van der Vliet, W. A., Huy, E. H., de Jong, P. J., Hamel, B. C. J., Schoneveld, A. H., Brunner, H. G., Veltman, J. A., & van Geest, A. G. (2004). Mutations in a new member of the chromodomain gene family cause charge syndrome. *Nature Genetics*, 36(5), 955-957. <https://doi.org/10.1038/ng1407>

What is dysautonomia? Dysautonomia International. (n.d.). Retrieved May 4, 2021, from <http://www.dysautonomiainternational.org/page.php?id=34>