

CLOCK GENE EXPRESSION IN CLUSTER HEADACHE

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INTRODUCTION

- **CLUSTER HEADACHE (CH)** is a rare headache disorder in which one of its most striking features is circannual and circadian patterns, having a seasonal incidence of its bouts in the spring and autumn and a daily clockwise regularity of attacks.
- The **CLOCK gene (CLOCK)** is the principal gene regulating the molecular mechanism of the mammalian circadian clock. Single nucleotide polymorphisms (SNPs) of rs12649507, related to sleep duration, have been associated with CH in a Swedish patient sample⁽¹⁾
- Other CLOCK polymorphisms were investigated in Cluster Headache - the 3092 T-C (also known as 3111 TC) related to modulation of sleep cycles in healthy subjects and to circadian mood fluctuations in patients with bipolar depression was not found in the two Italian Cluster Headache samples^(2,3), and CLOCK (rs1801260) was also not found to differ from controls in a Chinese Cluster Headache sample⁽⁴⁾.
- **CLOCK gene** expression levels were not found to differ from controls, although its expression was dependent on the rs12649507 phenotype⁽¹⁾

OBJECTIVE Evaluate CLOCK expression in CH patients (within and outside bouts) over the four seasons compared to controls.

METHODS

- Blood samples for CLOCK expression were collected sequentially 2 to 4 times over one year in chronic and episodic CH regardless of disease activity. Samples were scheduled to be taken always in the morning, 7 to 9 days after each solstice an equinox.
- Project started on December 2017 and will end in December 2019
- Clock gene expression was quantified in peripheral blood mononuclear cells (PBMCs) by quantitative real time PCR of mRNA using the primers: CLOCK_Forward TGCGAGGAACAATAGACCCAA ; CLOCK_Reverse ATGGCCTATGTGTGCGTTGTA
- Relative CLOCK expression of each sample was determined using the internal control GAPDH and then normalized to the average of the control population.

RESULTS

Interim analysis of the first **150 samples** of **50 participants**

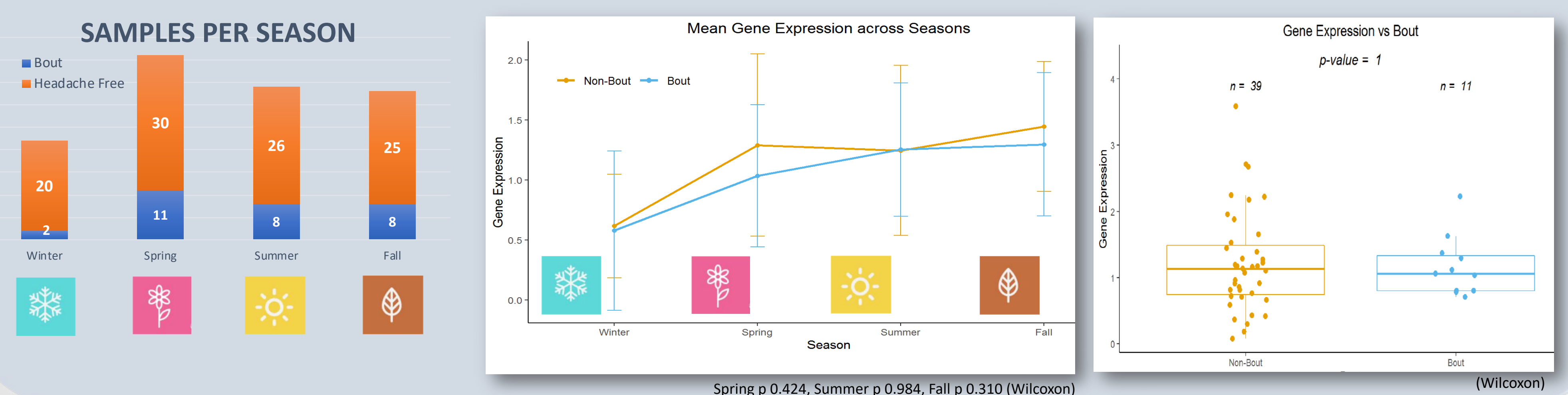
N = 53, 3 PATIENTS EXCLUDED (no samples collected)

PATIENTS	Gender (♀ : ♂)	8 : 42 (84%)
	Average Age	44.6 ± 13.5
Cluster (Episodic : Chronic)	47 (94%) : 3	
CONTROLS	Gender (♀ : ♂)	5 : 18 (78%)
	Average Age	41.6 ± 13.1
NO DIFFERENCES* IN Age / Gender		

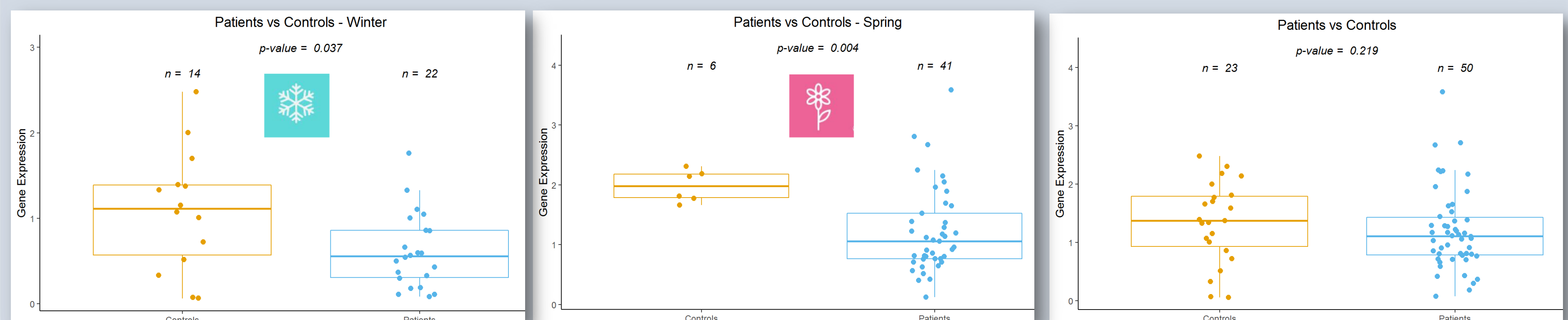
* T Test (p 0.379) // Fisher (p 0.532)

PATIENTS	SAMPLES COLLECTED			
	One	Two	Three	Four
9 Dropped Out	6	3	-	-
33 Completed	-	-	8	25
8 In Study	1	2	5	-

CLOCK EXPRESSION IN PATIENTS



CLOCK EXPRESSION IN PATIENTS vs CONTROLS



DISCUSSION

- **CLOCK gene expression** in **Cluster Headache** patients does not vary significantly across seasons nor does it seem to be influenced by disease activity (within or outside bouts).
- **CLOCK gene expression** was not different in **Cluster Headache** patients when compared to controls, as a group.
- When analyzing **CLOCK gene expression** in each season, **Cluster Headache** patients seem to have lower expression during the winter and spring. Further data is needed to confirm these findings and to related them to genotype differences⁽¹⁾.

REFERENCES

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