Treatment Outcomes in Temporomandibular Disorders Patients with Respect to Specific Genotypes

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BACKGROUND

To evaluate whether specific single nucleotide polymorphisms (SNPs) in pain-related genes have an impact on treatment outcomes after six months of treatment with stabilisation splint in patients suffering from pain-related temporomandibular disorders (TMDp) (Figure 1).

GGACGA**[A/G]**TGTGTA

Figure 1. SNP of *COMT* (rs4646310) represents gene variants with A or G allele. (https://www.thermofisher.com/order/genomedatabase/details/genotyping)

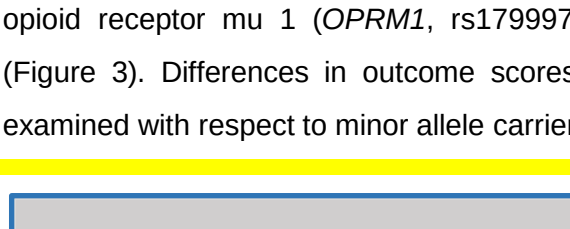

Figure 2. Sampling Swabs of Buccal Mucosa for DNA Isolation

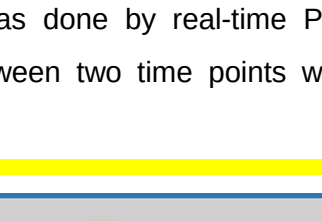

Figure 3. Pipetting DNA Samples for Genotyping

METHODS

Sixty TMDp patients (55F, 5M; 31.8 ± 11.7 yrs) were diagnosed according to DC/TMD. In all patients, diagnosis of myalgia, arthralgia or both were confirmed as well, as pain that lasted for six months.

All patients were treated with maxilary **stabilisation splint** for six months. All splints were made in articulator of hard acrylic with a thickness of 2 mm at the level of the first molar and adjusted before giving to patients.

Treatment outcomes, assessed at baseline (T0) and at 6th-month follow-up (T1), included range of mouth opening (**pain-free** referring to the extent to which a person can open their mouth without experiencing any discomfort and **maximum** mouth opening which refers to the widest possible distance a person can open their mouth, regardless of any discomfort), pain intensity (evaluated using Graded Chronic Pain Scale_GCPS), and anxiety symptoms (using Generalized Anxiety Disorder-7_GAD-7).

Buccal swabs were used to isolate DNA (Figure 2). Genotyping of genes encoding catechol-o-methyltransferase (*COMT*, rs4646310 and rs6269) and opioid receptor mu 1 (*OPRM1*, rs1799971) was done by real-time PCR (Figure 3). Differences in outcome scores between two time points were examined with respect to minor allele carriers.

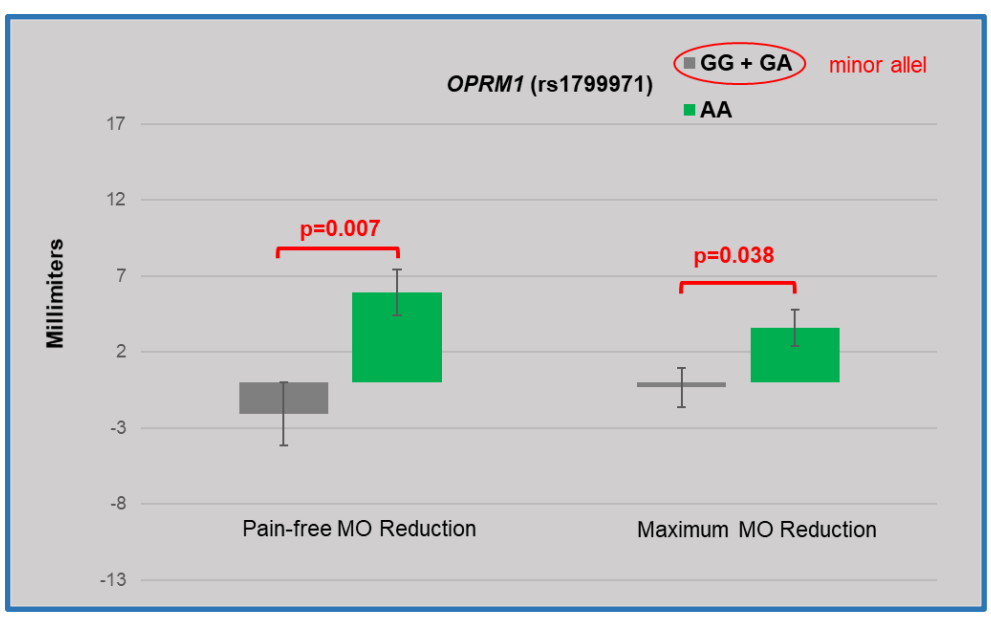

Figure 4. Pain-free and Maximum Mouth Opening (MO) After Six Months of Stabilisation Splint Therapy with Respect to Certain Genotype of *OPRM1* (rs1799971)

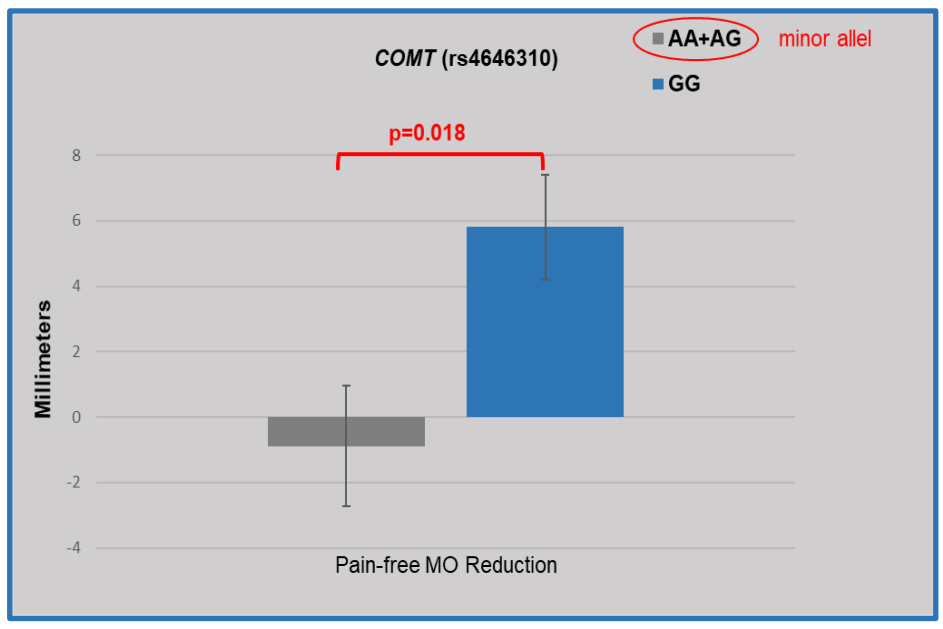

Figure 5. Reduction of Pain-free Mouth Opening (MO) After Six Months of Stabilisation Splint Therapy with Respect to Genotype of *COMT* (rs4646310)

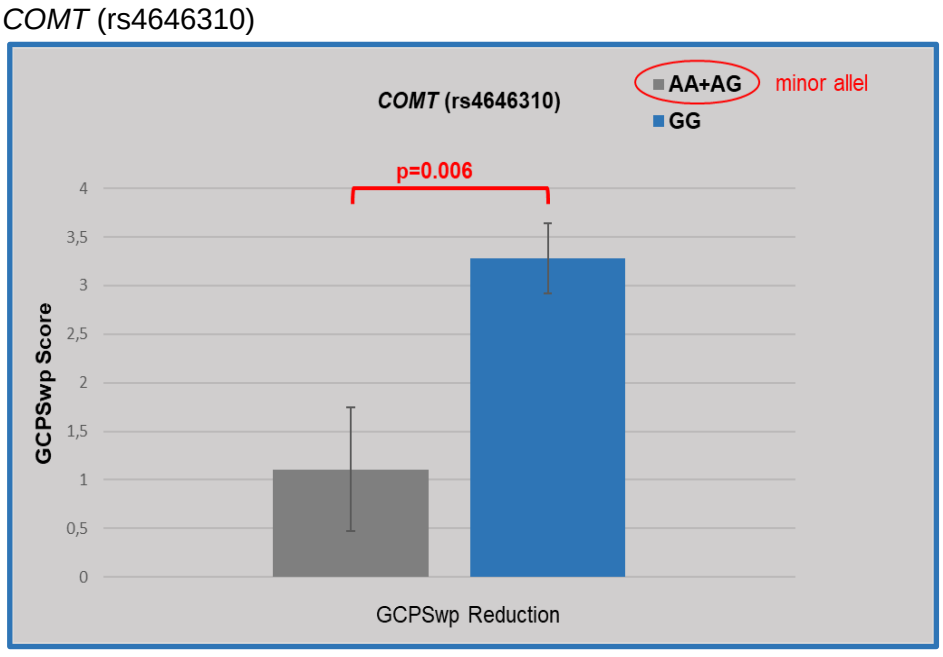

Figure 6. Reduction of Worst Pain Assesed by Graded Chronic Pain Scale (GCPSwp) After Six Months of Stabilisation Splnt Therapy with Respect to Genotype of *COMT* (rs4646310)

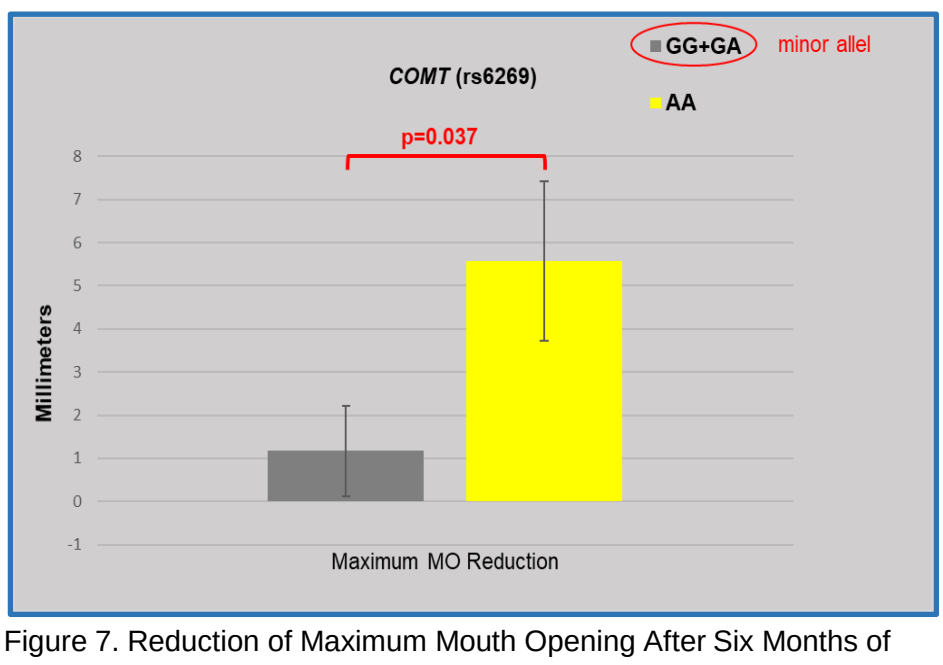

Figure 7. Reduction of Maximum Mouth Opening After Six Months of Stabilisation Splint Therapy with Respect to Genotype of *COMT* (rs6269)

RESULTS

When evaluating rs1799971 *(OPRM1)*, **minor allele carriers (GG+GA)** exhibited worsening in mouth opening while participants carrying AA genotype showed improvement (pain-free: -2.07 vs. 5.91mm, p=0.007; maximum: -0.33 vs. 3.59mm, p=0.038) (Figure 4).

When evaluating rs4646310 (*COMT*), **minor allele carriers (AA+AG)** reported significantly less pain reduction (GCPS_worst pain: 1.11 vs. 3.28, p=0.006), less anxiety reduction (-1.64 vs. 1.13, p=0.003) when compared with GG carriers. Also, minor allele carriers exhibited worsening in mouth opening while GG participants showed improvement (pain-free: -0.88 vs. 5.80 mm, p=0.018) (Figure 5,6).

When evaluating rs6269 (*COMT*), **minor allele carriers (GG+GA)** exhibited less improvement of maximum mouth opening when compared with AA carriers (1.17 vs. 5.57 mm, p=0.037) (Figure 7).

CONCLUSION

In general, minor allele carriers of evaluated genes exhibited less improvement after stabilisation splint therapy both in functional (pain-free and maximum mouth opening) and psychosomatic (pain and anxiety) treatment outcomes. Further research is needed to elucidate this connection.

FUNDING

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