




# SEX DIFFERENCES IN THE IMPACT OF TARGETED MIGRAINE TREATMENTS ON ASSOCIATED OBSESSIVE-COMPULSIVE TRAITS

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**Background.** Psychiatric comorbidities associated with migraine differ between men and women. While sex differences in anxiety and depression have been extensively investigated, obsessive–compulsive (OC) traits remain poorly explored. Although targeted therapies, including anti-calcitonin gene-related peptide monoclonal antibodies (anti-CGRP mAbs) and Onabotulinumtoxin-A (OBT-A), effectively reduce migraine burden, their impact on OC traits and potential sex-specific differences remains unclear.

**Aims.** To evaluate the effect of targeted migraine therapies on OC traits and investigate sex differences in treatment-related changes.

**Methods.** Consecutive patients attending the tertiary Headache Center of the Neurological Clinic, AOU delle Marche, who initiated anti-CGRP mAbs or OBT-A were prospectively enrolled. Participants completed the Obsessive–Compulsive Inventory-Revised (OCI-R) at baseline (T0) and after one year (T1). OCI-R categories at T1 were analysed using a full-factorial multinomial logistic regression model including baseline OCI-R, sex, and their interaction.

**Results.** Ninety patients were included. Overall, targeted therapy was associated with a shift toward lower OCI-R severity categories at T1. Multinomial logistic regression identified significant sex-by-baseline OCI-R interactions for Class 3 versus Class 1 ($\beta = 13.33$, $p<0.001$) and Class 4 versus Class 1 ($\beta = -7.77$, $p<0.001$), whereas no interaction was observed for Class 2 versus Class 1 ($p = 0.981$). At low baseline OCI-R values (mean −1SD), the probability of remaining in the lowest OCI-R class was similar in men (95.0%) and women (94.2%). At higher baseline OCI-R values (mean +1SD), this probability declined to 77.5% in men and 64.8% in women. Concurrently, women showed a progressive increase in the probability of belonging to the most severe OCI-R class (13.3%), whereas men mainly transitioned to Class 2 (22.5%), with the probability of the most severe class increasing only at the highest OCI-R levels.

**Conclusions.** Targeted migraine therapies were associated with an overall improvement in obsessive–compulsive symptoms. However, sex significantly moderated the relationship between baseline OC symptom severity and longitudinal symptom trajectories, revealing distinct patterns of symptom evolution in men and women. These findings underscore the importance of considering sex-specific psychiatric phenotypes in migraine and support the integration of neuropsychiatric profiling into personalised therapeutic strategies.