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Omega-3 Supplementation Prevents Stress-Induced Increases in Ethanol Consumption in Male and Female Mice

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Introduction

Social stress is a well-established risk factor for alcohol use disorders, increasing vulnerability to alcohol consumption and promoting excessive drinking behaviors. Conversely, omega-3 deficiency may arise from multiple factors, including excessive alcohol consumption. This concern is further supported by the marked shift in Western dietary patterns toward a highly imbalanced omega-6/omega-3 ratio (20–30:1), which may contribute to the prevalence and consequences of omega-3 deficiency.

Material and methods

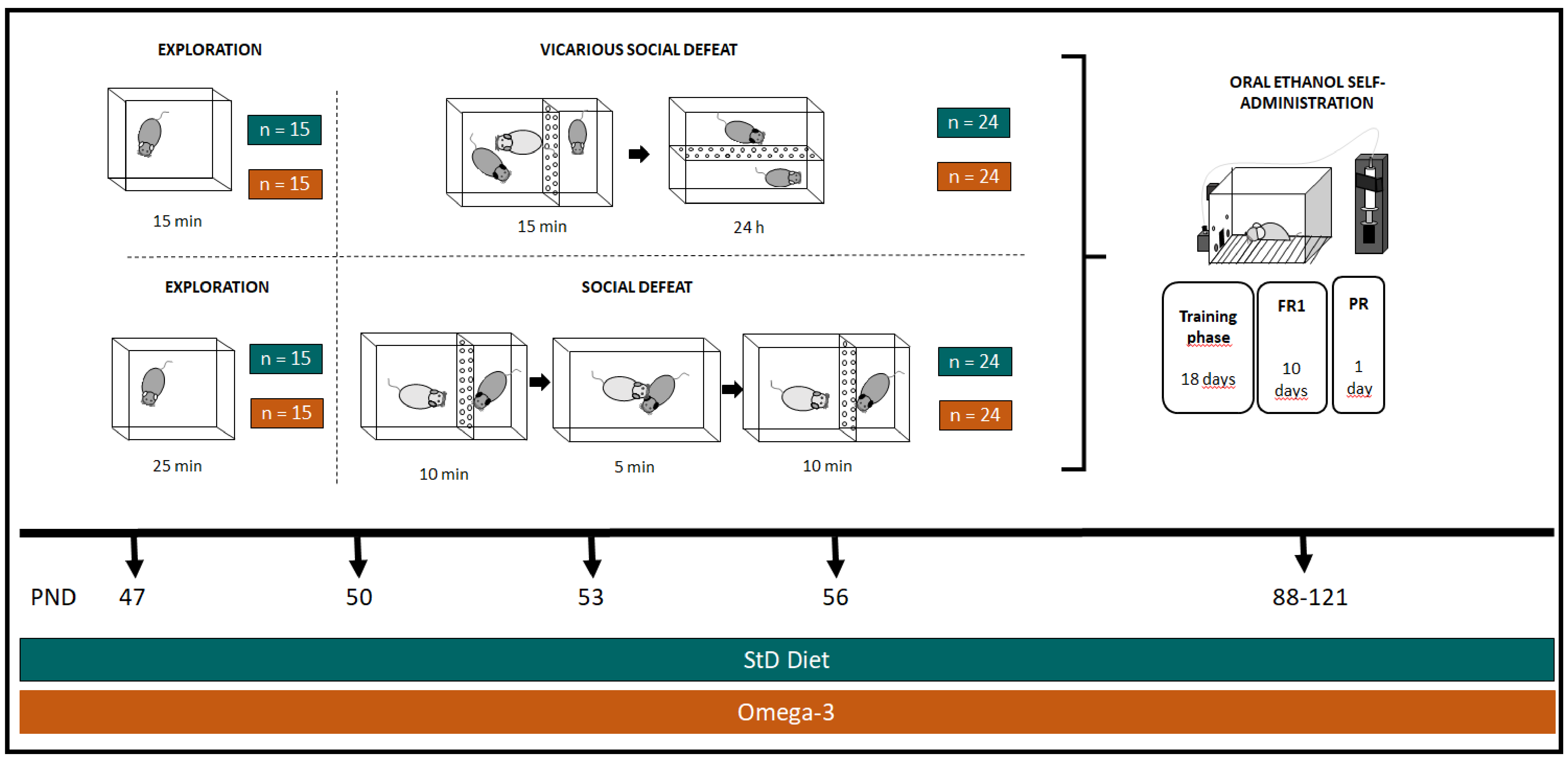
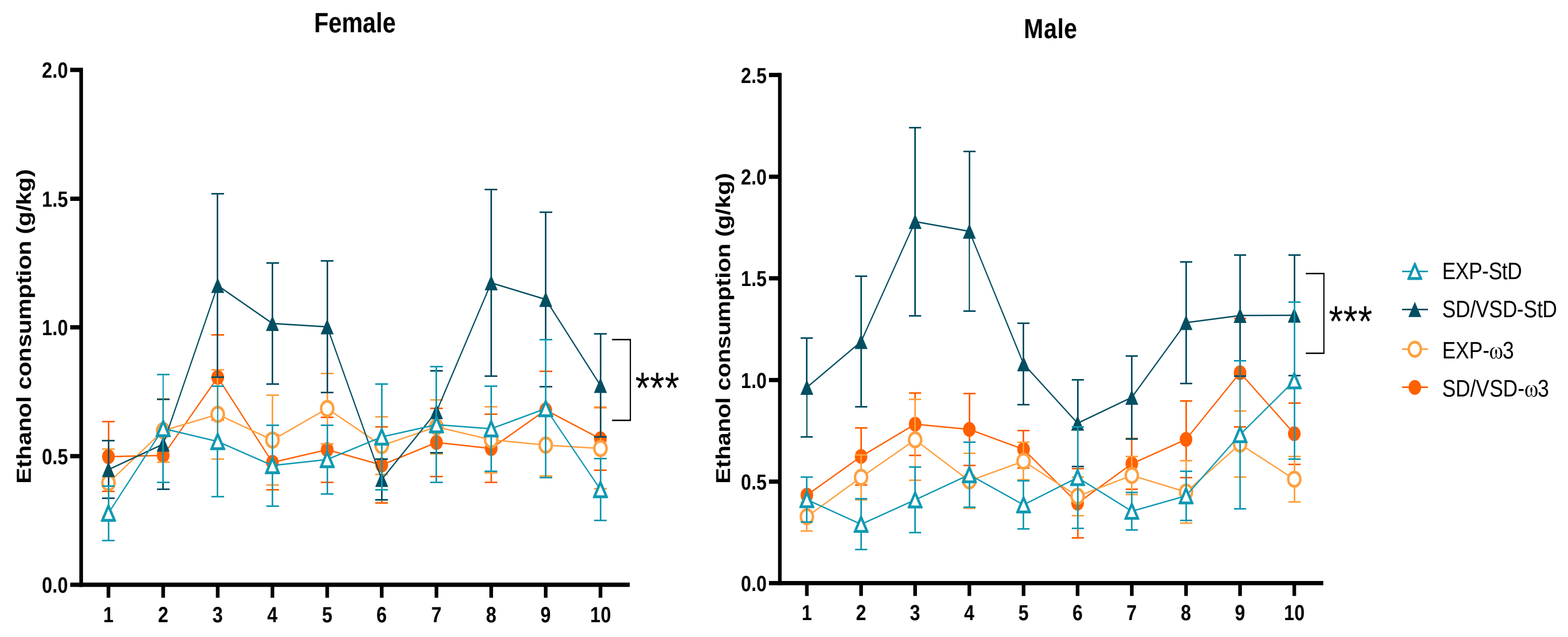


Figure 1. Experimental desing

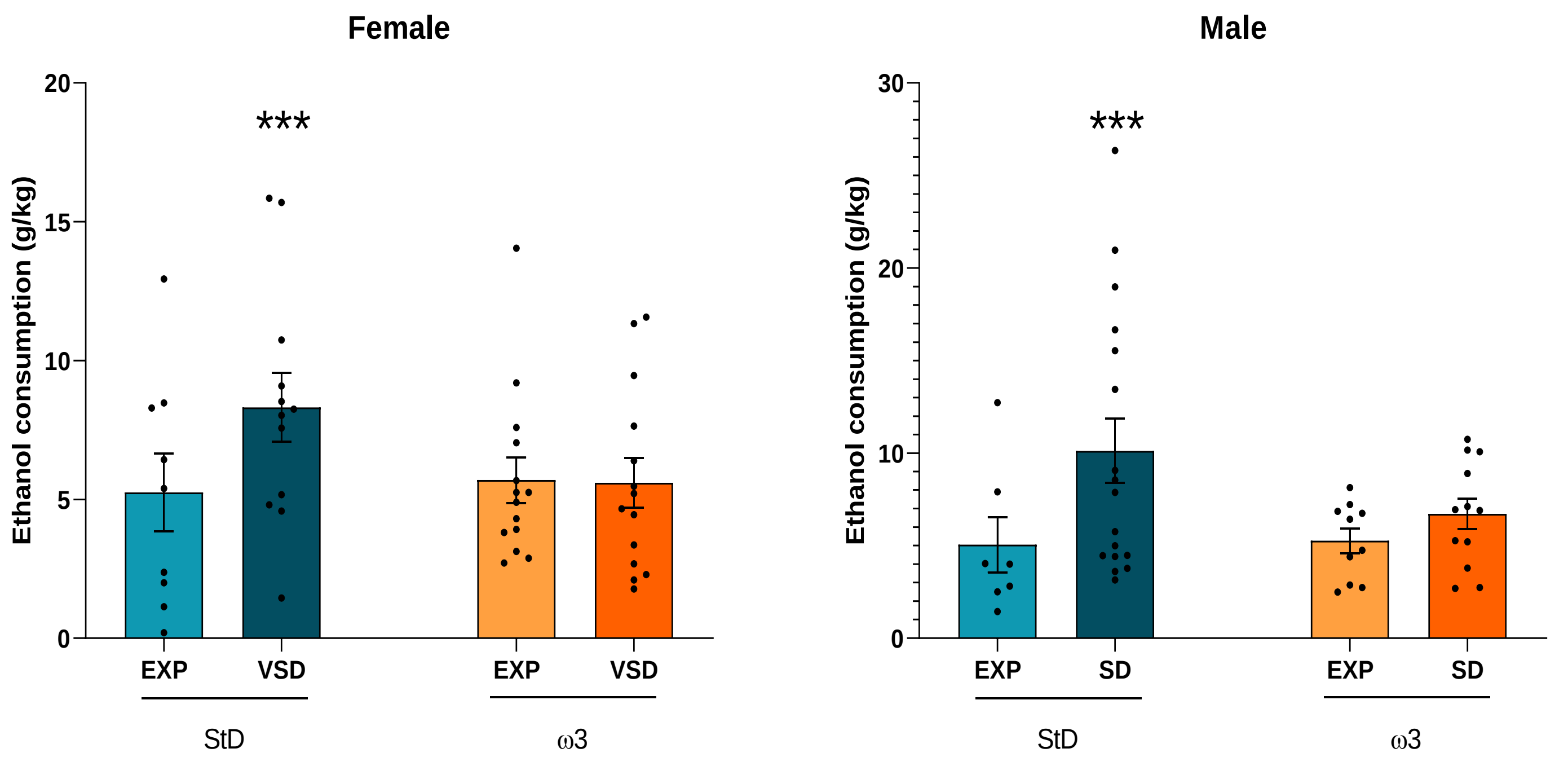
A total of 156 OF1 mice (78 males, 78 females) were assigned to either an omega-3–enriched or standard diet and exposed to one of two stress conditions: non stressed (exploration) or stressed (social defeat for males and vicarious social defeat for females. The omega-3 diet was administered from postnatal day (PND) 21 throughout the study, while stress exposure occurred on PND 47, 50, 53, and 56. Ethanol intake was assessed using oral ethanol operant self-administration with FR1 phase (10 days). Motivation for ethanol seeking was subsequently evaluated in a Progressive Ratio (PR) task, with the breaking point defined as the highest response requirement completed to obtain reinforcement.

Results

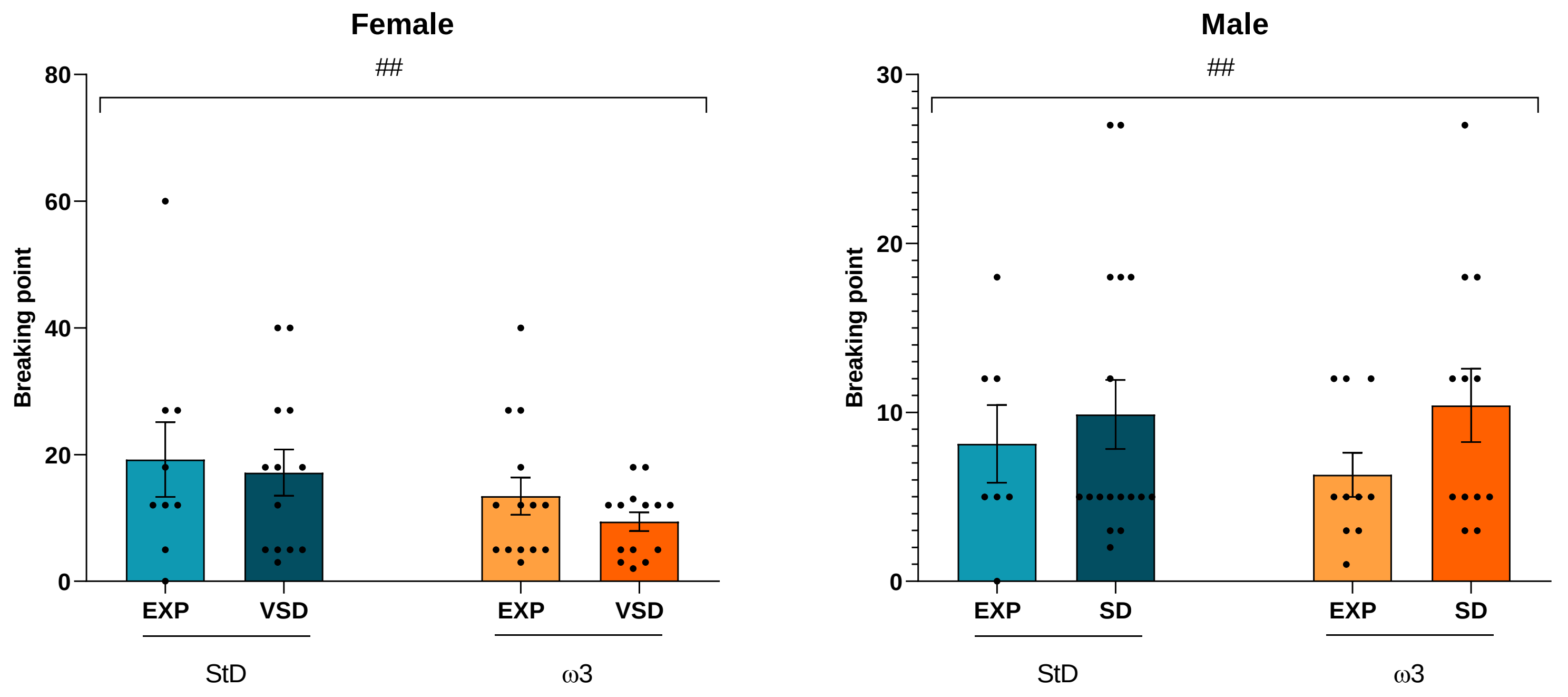
A) FR1 ethanol consumption per days



B) Total etanol consumption diring FR1



C) Breaking point in the PR fase



D) Total etanol consumption during the PR

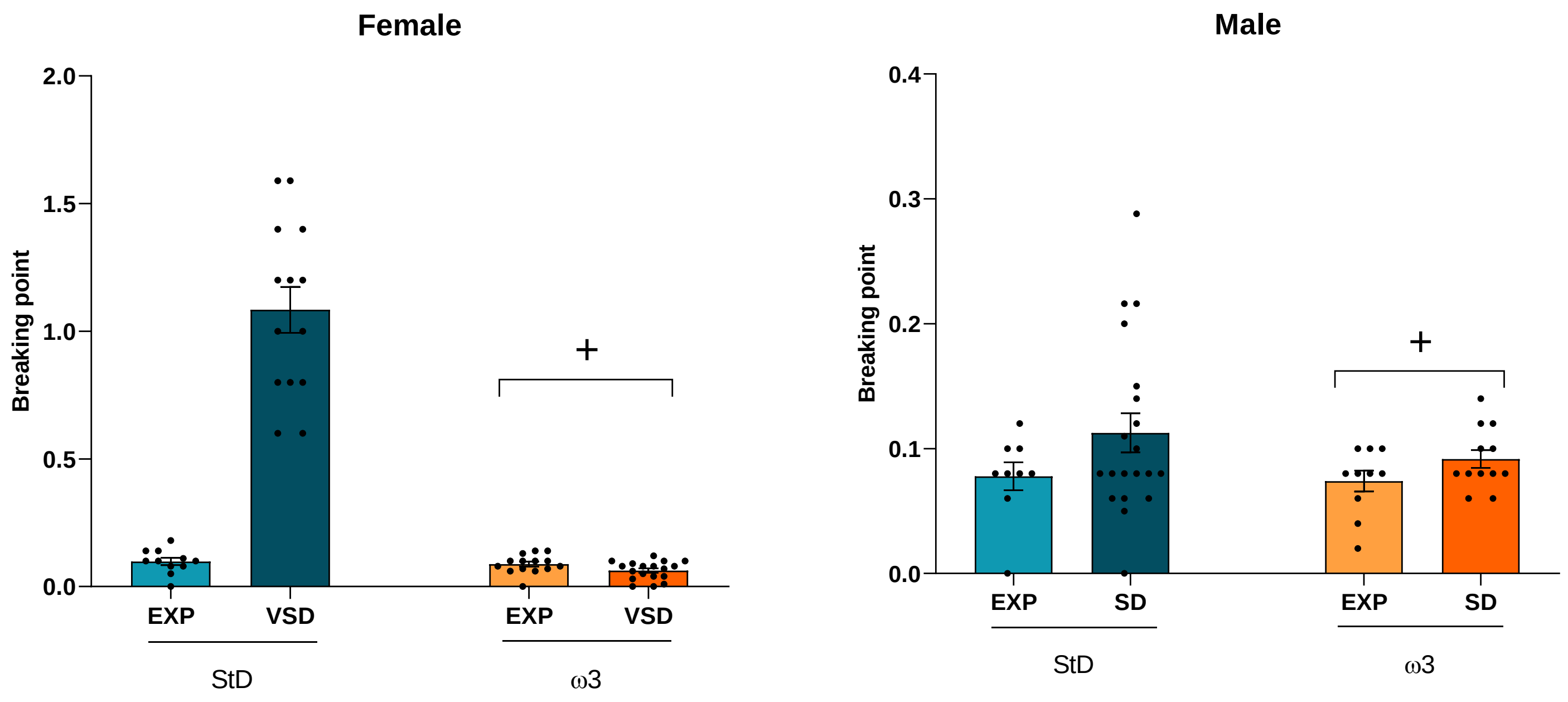


Figure 2. Results

A) *Fr1 ethanol consumption per days.* *** $p < 0.001$ significant differences compared with the rest of the groups. B) *Total ethanol consumption during FR1*. *** $p < 0.001$ significant differences compared with the rest of the groups. C*) Breaking point in the PR fase*. ## $p < 0,01$ significant differences between sexes. D) Total ethanol consumption during the PR. + $p < 0,05$ with respect the StD diet.

Conclusion: Social stress increases initial ethanol consumption in both sexes, an effect successfully counteracted by omega-3 supplementation. Furthermore, females exhibit higher motivation for ethanol, while omega-3 broadly reduces overall alcohol consumption during the progressive ratio phase regardless of sex.

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