DHA ameliorates repeated stress induced-chronic pain via GPR40/FFAR1

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Aims; We previously reported that the duration of postsurgical pain was prolonged by the exposure of repeated-social defeat stress (RSDS), and the prolongation was ameliorated by docosahexaenoic acid (DHA). G-protein coupled receptor 40/free fatty acid receptor 1 (GPR40/FFAR1), which is activated by long chain fatty acids, has beneficial effect to pain and emotion. In this study, we examined the involvement of DHA-GPR40/FFAR1 signaling in RSDS induced-chronic pain.

Methods; GPR40/FFAR1 wild type (GPR40^{wt}) and knockout (GPR40^{ko}) mice (9 weeks old) were exposed RSDS. Postsurgical pain was induced by plantar incision. Vehicle or DHA (25 mmol/kg) was orally administrated once a day during RSDS. Paw withdrawal thresholds (PWT) were evaluated using by von Frey filaments.

Results; In RSDS-GPR40^{wt}, vehicle or DHA treated mice showed decrease of PWT on day 1 after paw surgery. However, on day 7 after paw surgery, decrease of PWT disappeared in DHA treated mice but not vehicle treated mice. In RSDS-GPR40^{ko}, decrease of PWT occurred on day 1 after paw surgery. DHA did not ameliorate decrease of PWT in RSDS-GPR40^{ko} on day 7 after paw surgery.

Conclusion; DHA-GPR40/FFAR1 signaling may be therapeutic target of chronic pain associated with emotional disorders.