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	exp	pression		3	2	B n	rain reg pFC, Al	ions of MYG (w	intero vhere	est includ STR has

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induce dendritic changes), and CB (where no STR-induced changes are expected)

nic stress alters local estradiol expression oss brain regions in a sex-dependent way

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	After STR:
t	M: ↓ F: n.c.
	M: ↓ F: ↓

Goal 2: E2 Expression

Brain	E2 Expression after STR:					
region	Males:	Females:				
HIPP	Ť	mixed				
mPFC	~↓	~↑				
AMYG	~↑	~↑ n.c.				
СВ	n.c.					

Chronic stress tended to increase E2 expression in the male HIPP, female mPFC, and AMYG for males and females, and decrease E2 expression in the male mPFC.

Chronic stress may alter E2 production *WITHIN* the brain

ARO-L expression may be key in understanding sex-specific brain

responses to chronic stress: ARO-L is necessary to convert T into E2

ARO-L may be a potential *COMPENSATORY* mechanism in the HIPP Males showed higher hippocampal ARO-L expression than did females and a pattern of chronic stress increasing ARO-L vs. control males Given that chronic stress leads to hippocampal dendritic retraction in males,

STR \longrightarrow $\stackrel{\wedge}{\longrightarrow}$ ARO-L \implies $\stackrel{\wedge}{\longrightarrow}$ local E2 synthesis?

• A pattern was observed with males showing decreased ARO-L mPFC

expression, while females showing increased ARO-L expression.

The mPFC is highly sensitive to chronic stress, undergoing dendritic changes

STR $\implies \stackrel{\downarrow}{\longrightarrow} \stackrel{\text{ARO-L}}{\text{expression}} \implies \stackrel{\downarrow}{\longrightarrow} \stackrel{\text{local E2}}{\text{synthesis?}}$

Local E2 synthesis in the brain may be a critical mechanism for structural and functional changes in response to chronic stress Will need to test by blocking E2 synthesis to confirm this hypothesis

• Inhibiting ARO-L (via letrozole), thus blocking E2 production, decreases HIPP dendritic

• Both male and female ArKO (Aromatase-deficient) mice show worse HIPP- and PFC-• Female ArKO mice show higher depressive-like behavior than wild-type [4]

MDD may be associated with altered local E2 synthesis across brain regions

• Hormone-based breast cancer chemotherapy that inhibits aromatase (such as

• Future directions: region-specific hormonal mechanisms underlying MDD,

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