

Chronic flibanserin treatment increases solicitations in the female rat.

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Background

- **Hypoactive sexual desire disorder (HSDD)** : prevalent disorder in pre- and postmenopausal women
- **Flibanserin** currently in Phase III, developed for the treatment of HSDD in women
- Proposed relevant experimental model for further **flibanserin** preclinical studies : measure of **proceptive** behaviors in the **female rat**
 - but needs further validation for use as predictive model

Female rat sexual behavior

APPETITIVE / PROCEPTIVE behaviors

Related to **SEXUAL MOTIVATION**



- genital investigation
- ear wiggling
- active solicitation
- hops and darts
- pacing

Homologous to women sexual desire

CONSUMMATORY / RECEPTIVE behaviors

Related to **COPULATION**



- lordosis response :
 - lordosis quotient
 - lordosis intensity

No counterpart to women sexual response

Objective

Aim :

To assess the effects of flibanserin treatment on female rat sexual behavior.

General procedure :

Measure of proceptive and receptive behaviors in female rats during copulatory tests with sexually active male rats, in bilevel chambers.

Methods

1. 52 sexually naive Long Evans female rats
2. Females are **ovariectomized** and rendered **sexually receptive** by hormonal priming : estradiol (10µg) and progesterone (500µg) administered 48h and 4h respectively before the copulatory test.
3. **10 sexual training tests** (T1 to T10) (30min) with sexually active males
4. **4 treatment groups** (p.o., twice a day, for 29 days):
 - Flibanserin 5 mg/kg
 - Flibanserin 15 mg/kg
 - Flibanserin 45 mg/kg
 - Vehicle (0,5% Natrosol + 1% Polysorbate)
5. **5 treatment tests** : (T11 : acute treatment test, T12 to T15 : once a week)

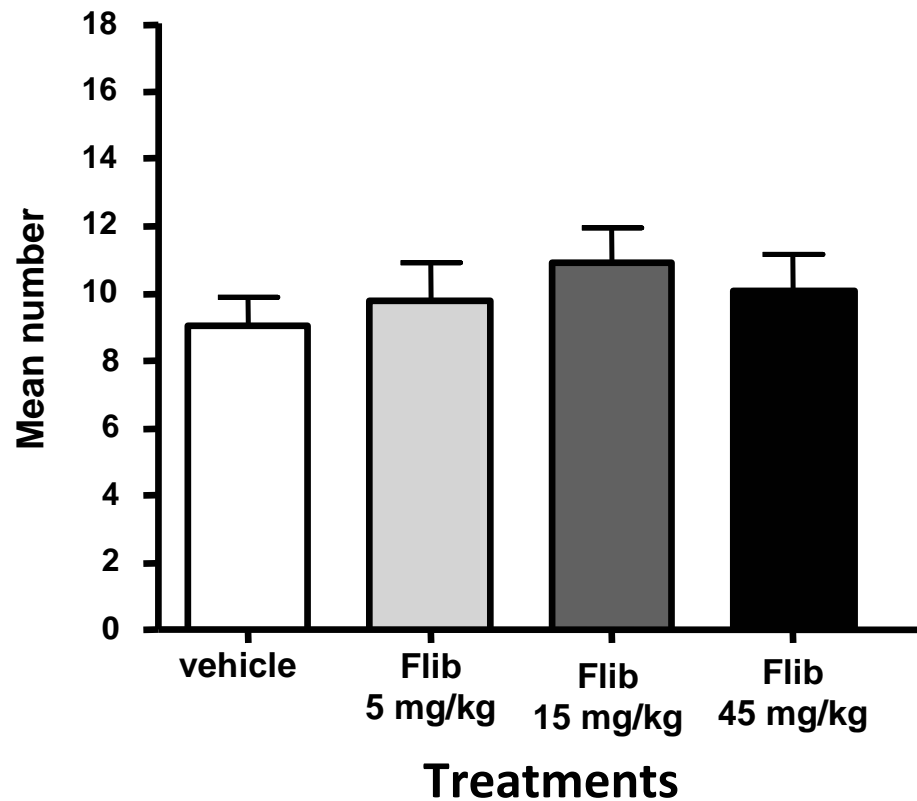
Methods

- All training and treatment tests videotaped and scored by experimenters blind to the treatment

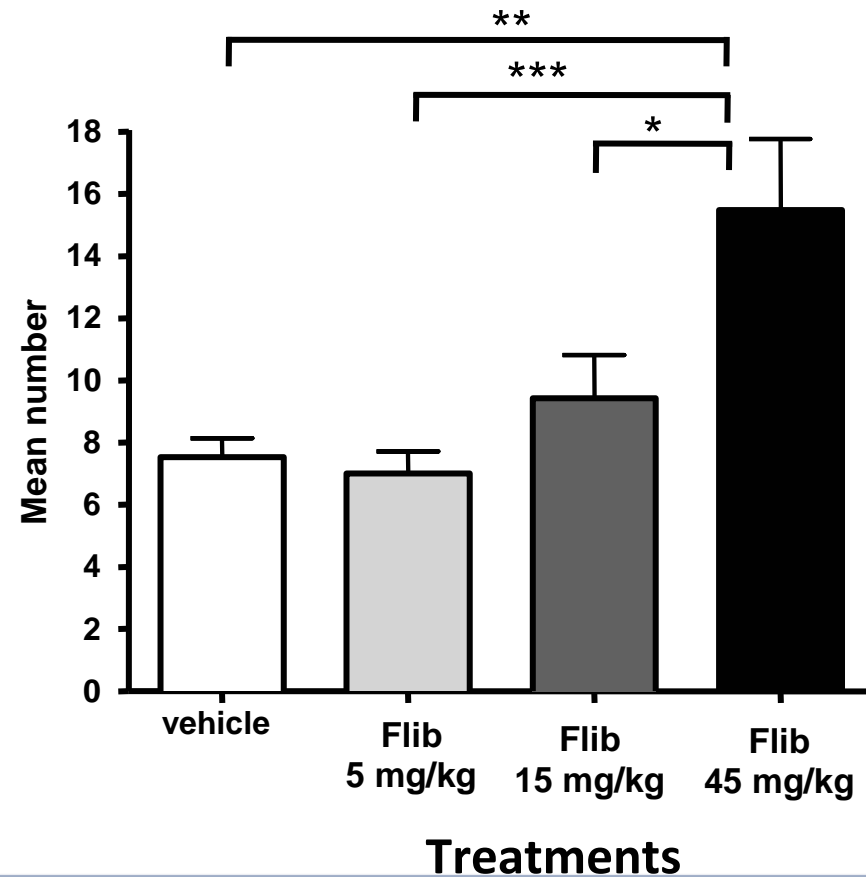


Flibanserin enhanced active solicitations toward males

Number of solicitations before beginning of treatment (Baseline)

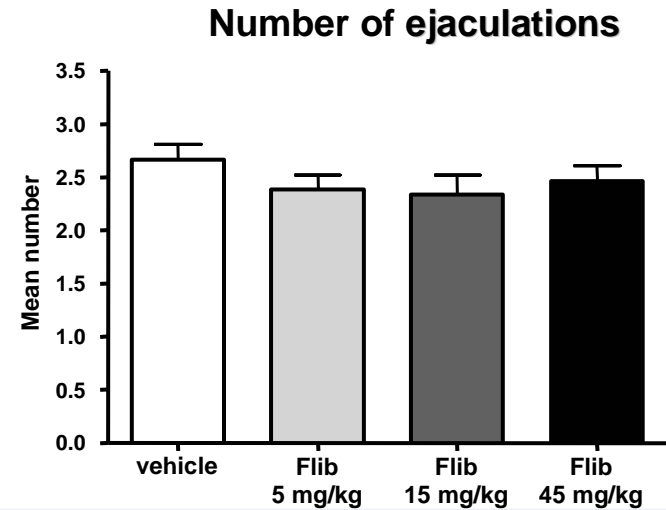
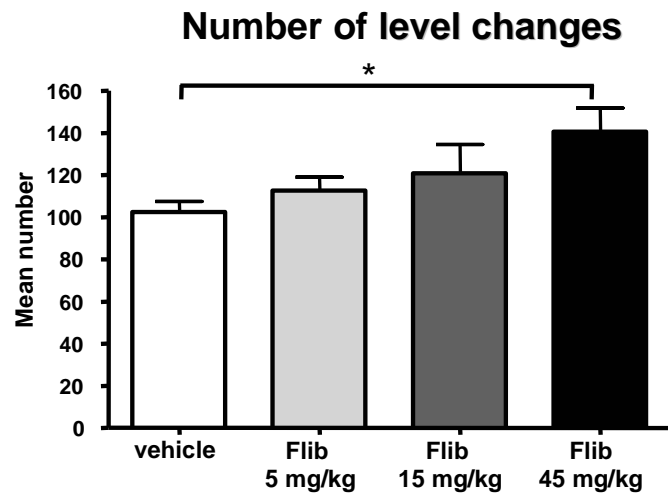
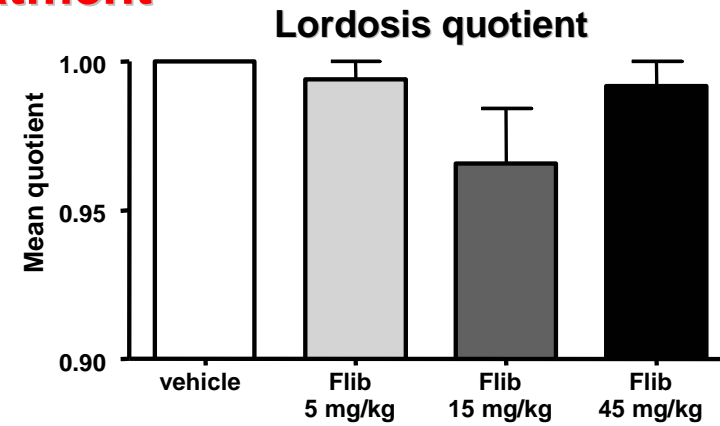
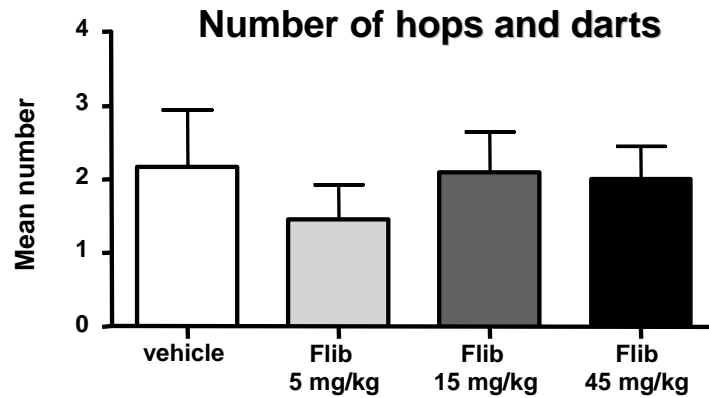


Number of solicitations after 15-days of treatment



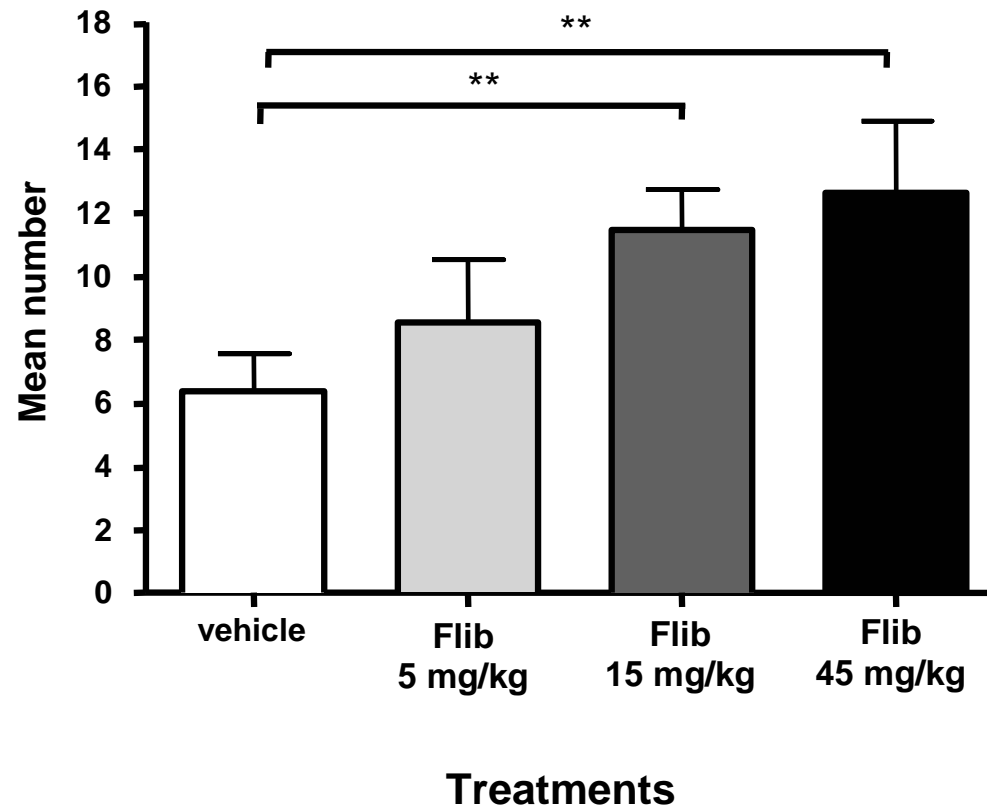
Flibanserin did not modify other behavioral parameters

after 15-days of treatment



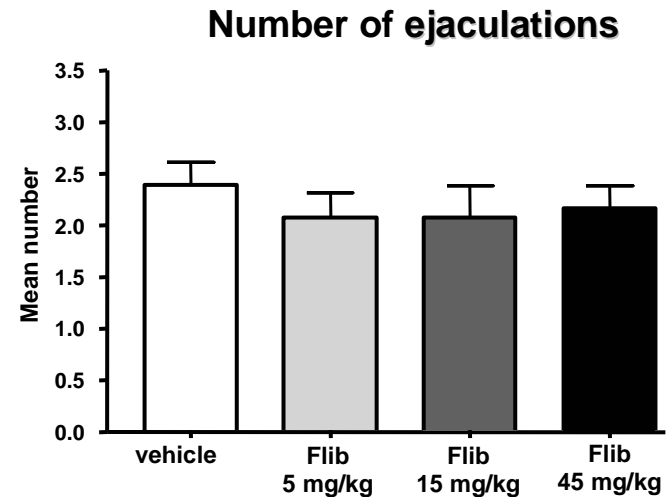
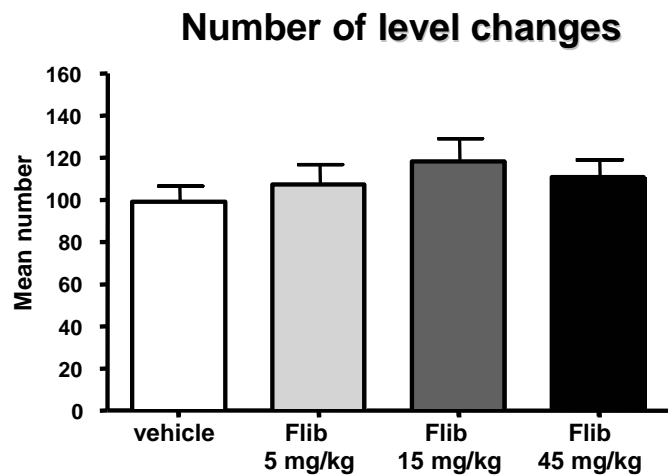
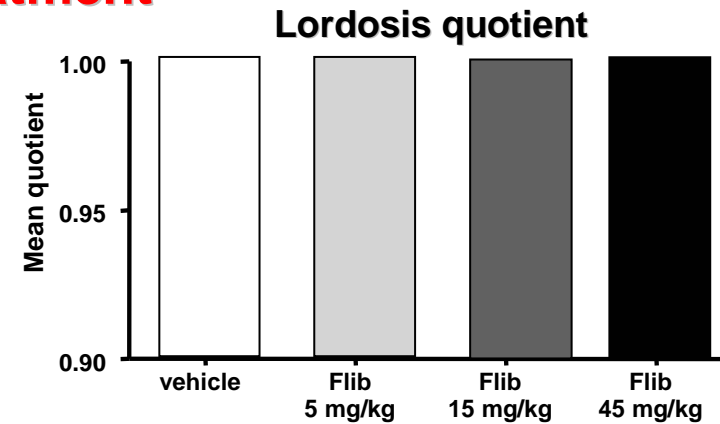
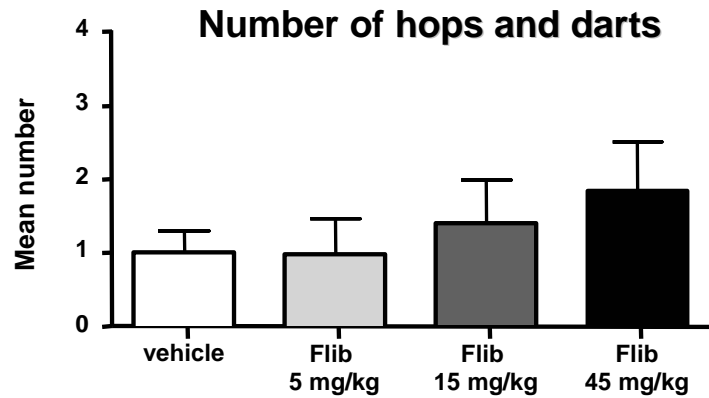
Flibanserin enhanced active solicitations toward males

Number of solicitations after 22-days of treatment



Flibanserin did not modify other behavioral parameters

after 22-days of treatment



SUMMARY

- **15-days** of chronic **45 mg/kg flibanserin** treatment results in a significant increase in female solicitations, compared to lower flibanserin doses (5 and 15 mg/kg) or vehicle
- This facilitatory effect of **45 mg/kg flibanserin** on female solicitations is still observed after **22-days** of chronic treatment
- Chronic flibanserin treatment did not modify **other** proceptive or receptive female sexual behaviors

CONCLUSION

These results evidence, for the first time, the prosexual effect of **flibanserin** in female rats receiving 45 mg/kg, twice daily administered for 15 days.

Since flibanserin has shown efficacy in treating premenopausal women with HSDD, these data combined suggest this **animal model** may be useful in supporting further pre-clinical drug studies for **female sexual dysfunction**.