



Effects of flibanserin on appetitive and consummatory aspects of sexual behavior in ovariectomized female rats primed with estrogen and progesterone

Kelly A. Allers¹, H el ene Gelez², Bernd Sommer¹ & Fran ois Giuliano^{2,3}

¹Boehringer Ingelheim Pharma GmbH – Germany

²Pelvipharm Laboratories – France

*³Dept. of Physical Medicine and Rehabilitation
Raymond Poincar e H opital, Garches,
Paris West Medical University – France*



Background

- **Flibanserin** a 5-HT1A agonist and 5-HT2A antagonist
- **Flibanserin** developed for the treatment of hypoactive sexual desire disorder (**HSDD**) in women
- Proposed relevant experimental model for further **flibanserin** preclinical studies : measure of **sexual appetitive** behaviors in the **female rat**

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 repeated flibanserin treatment on female rat sexual behavior.

General procedure :

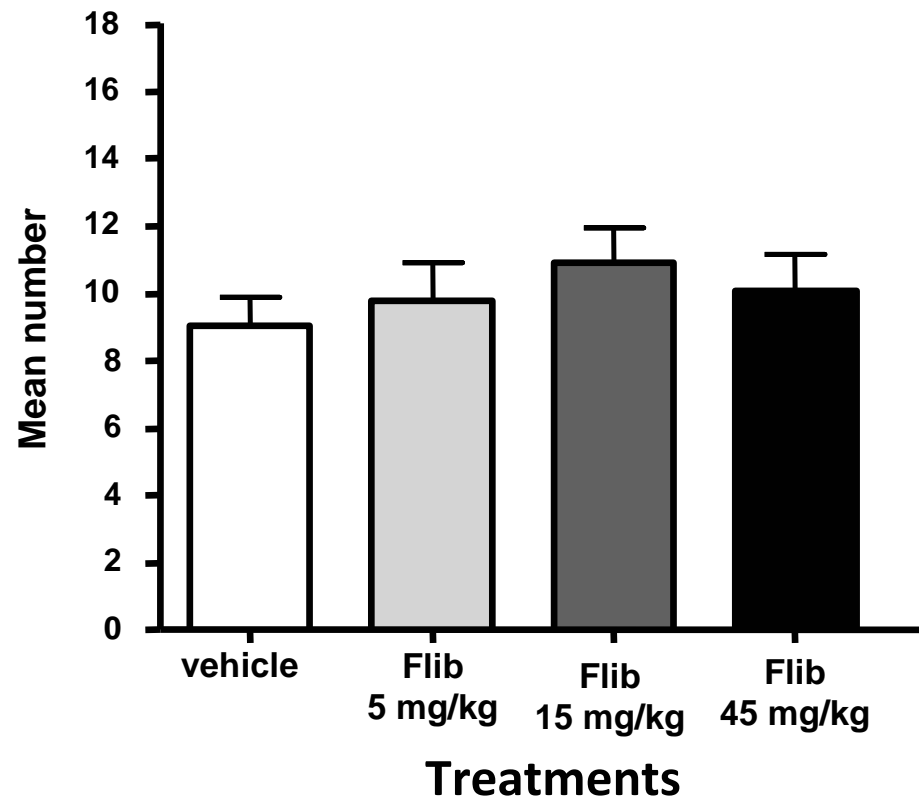
Measure of proceptive and receptive behaviors in female rats during copulatory tests with sexually active male rats, in bilevel chambers.

Methods

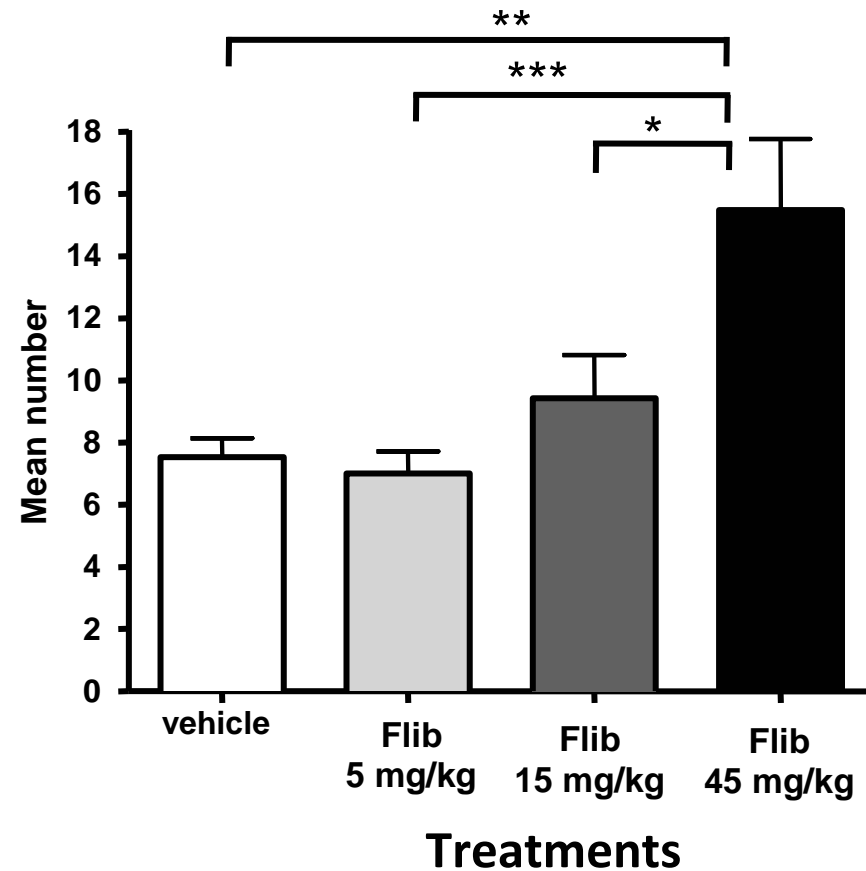
1. **52 sexually naive Long Evans female rats**
 2. Females are **ovariectomized** and rendered **sexually receptive** by hormonal priming : estradiol (10µg) and progesterone (500µg) administered 48h and 4h respectively before the copulatory test.
 3. **10 sexual training tests** (T1 to T10) (30min) 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)
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Flibanserin enhanced active solicitations toward males

Number of solicitations before beginning of treatment (Baseline)

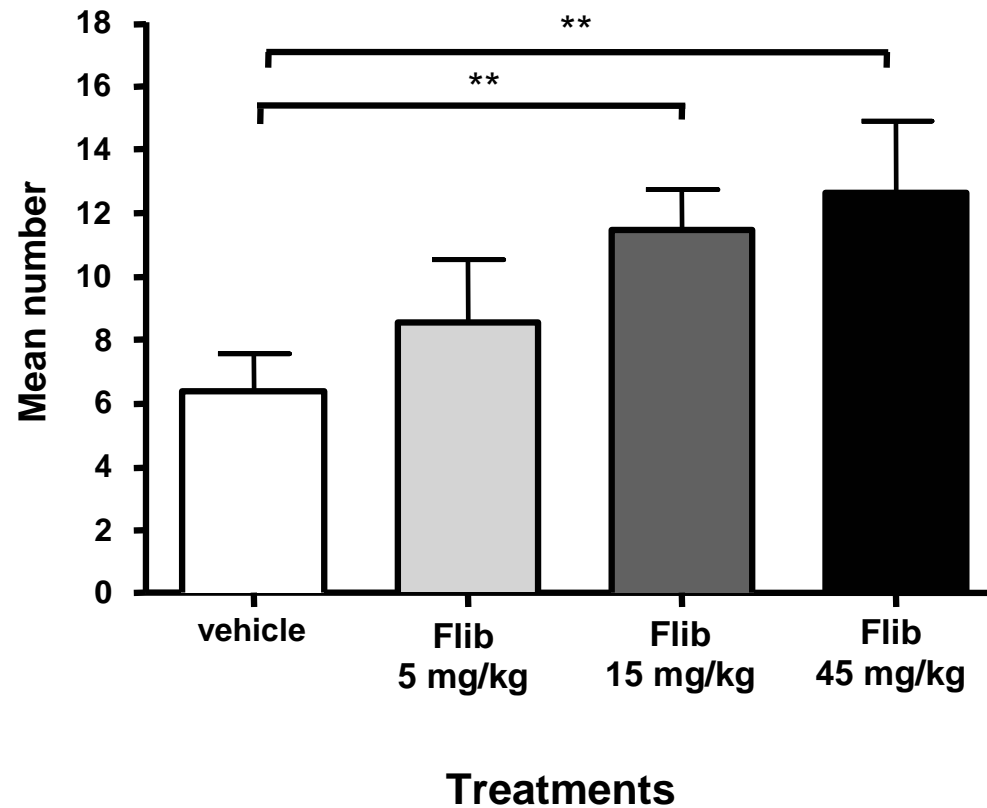


Number of solicitations after 15-days of treatment



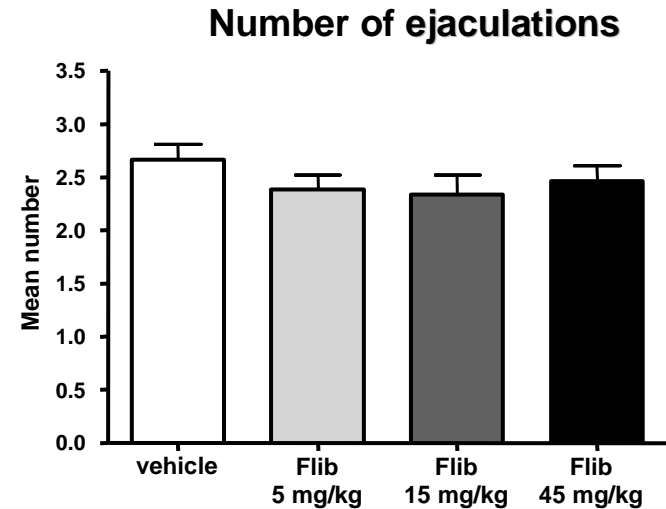
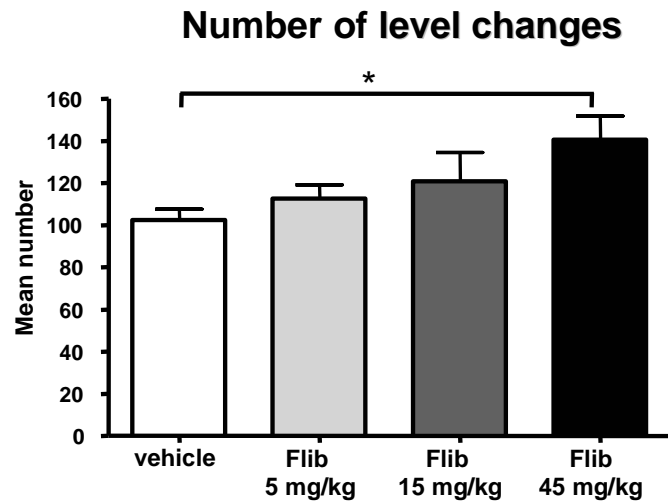
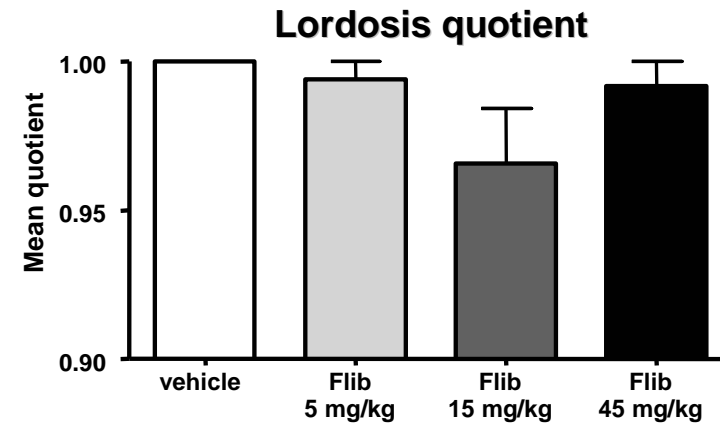
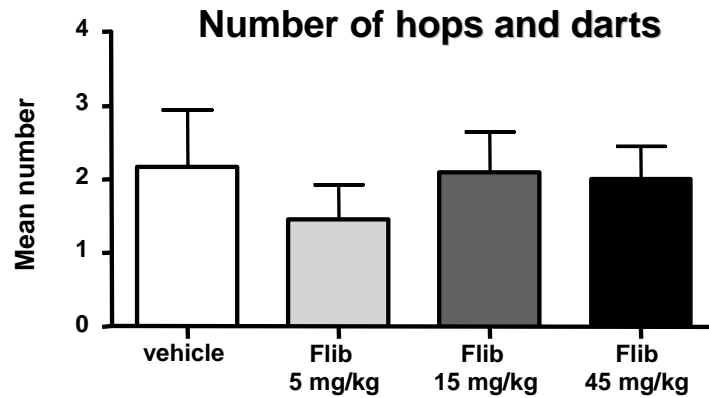
Flibanserin enhanced active solicitations toward males

Number of solicitations after 22-days of treatment



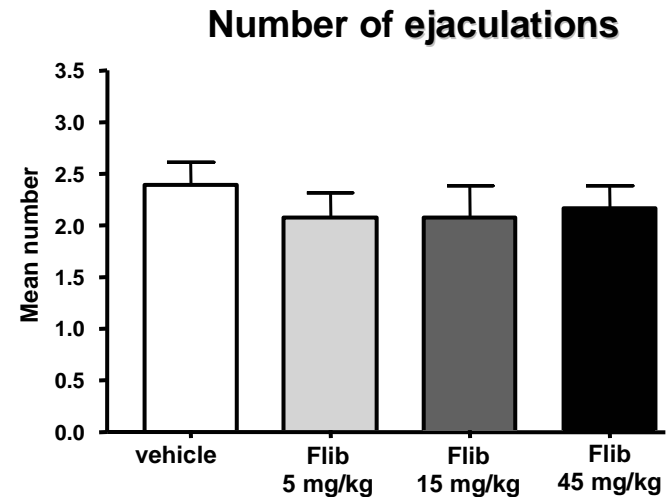
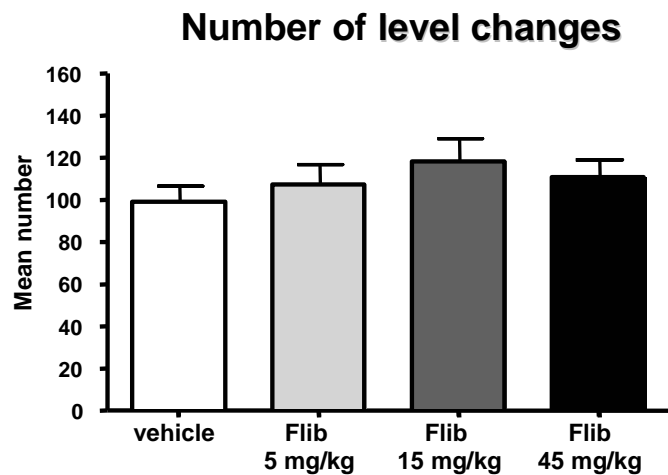
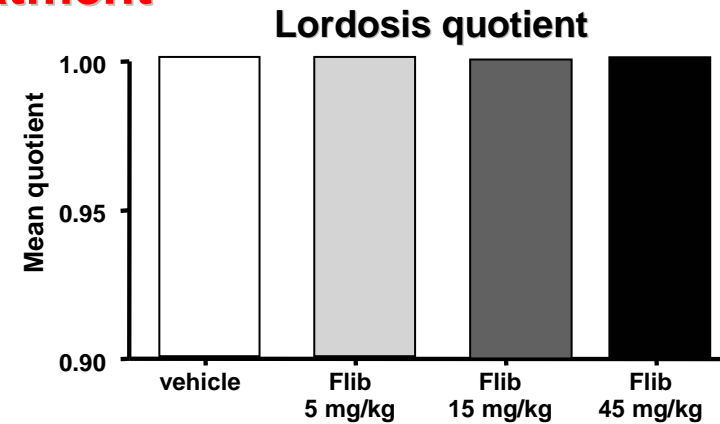
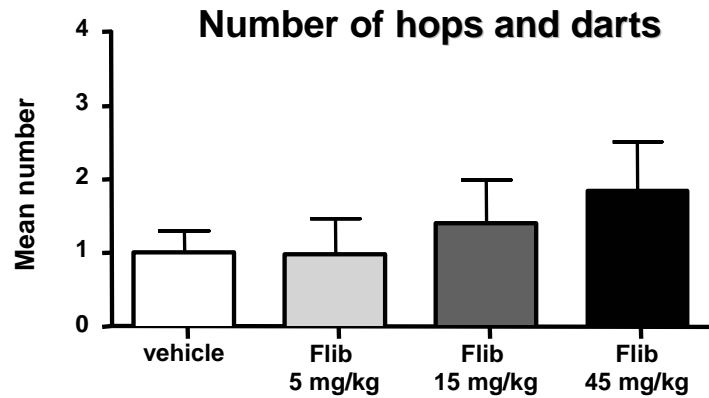
Flibanserin did not modify other behavioral parameters

after 15-days of treatment (same after 22-days)



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**.