

# EVALUATION OF RESPIRATORY DEPRESSION INDUCED BY FENTANYL IN RATS USING THE DECRO JACKETED TELEMETRY

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## Introduction

- Opioid-induced respiratory depression is potentially life threatening and the cause of substantial morbidity and mortality.
- DECRO<sup>®</sup> jacketed telemetry device allows to non-invasively monitor the respiratory function in combination with cardiac and activity level monitoring in rats [1-2]

**Aim of the study :** Evaluate assessment of opioid-induced respiratory depression in rodents with DECRO jacket.

## Material and methods

**Animals :** 4 Sprague Dawley adult rats (210-260 g) with two habituation to the jacket conducted the week before the experiment day as recommended in [2]

**Experimental Procedure :** Shearing in the dorsolateral region to prepare skin for ECG electrodes the day before the experiment. Equipping animals with the jacket as illustrated in Fig.1 and placing them into an individual experiment cage. Subcutaneous injection of Fentanyl 100 µg/kg after two hours of baseline. Jacket removal after 4 hours.

### Data Recording and Analysis (DECRO 1.0.0 software):

- Parameters detailed in Table 1 were recorded during 4 hours
- Data were analyzed and averaged every 15 min
- Relative variations expressed as % change versus pre-dose values taken during the last 30 min before dosing.

## Results

- Fentanyl induced an immediate respiratory depression with peak effect reached around 30 min (expected C<sub>max</sub>) : decrease of -57% for minute volume and -37% for respiratory rate
- Activity Level of the animals dropped of -83% (≤10 mg indicates completely inactive animals).
- The animals partially recovered their baseline levels from 90 min post-dose : -18% Respiratory Rate, -29% Minute Volume and -24% Activity Level
- No significant effect was observed for Heart Rate (data not shown)

	Sensor	Parameter	Pre-dose -0,5h*	C <sub>max</sub> 0,5h*	Recovery 1,75h*
Respiratory function	Respiratory inductive plethysmography (RIP) bands included in the jacket	RespR	166±2 (bpm)	-37±4 (%)	-18±5 (%)
		MV	335±22 (arb.u./min)	-57±3 (%)	-29±6 (%)
		VT	2,1±0,1 (arb.u.)	-33±2 (%)	-16±4 (%)
Activity	3D accelerometer	AL	47±4 (mg)	-83±1 (%)	-24±27 (%)

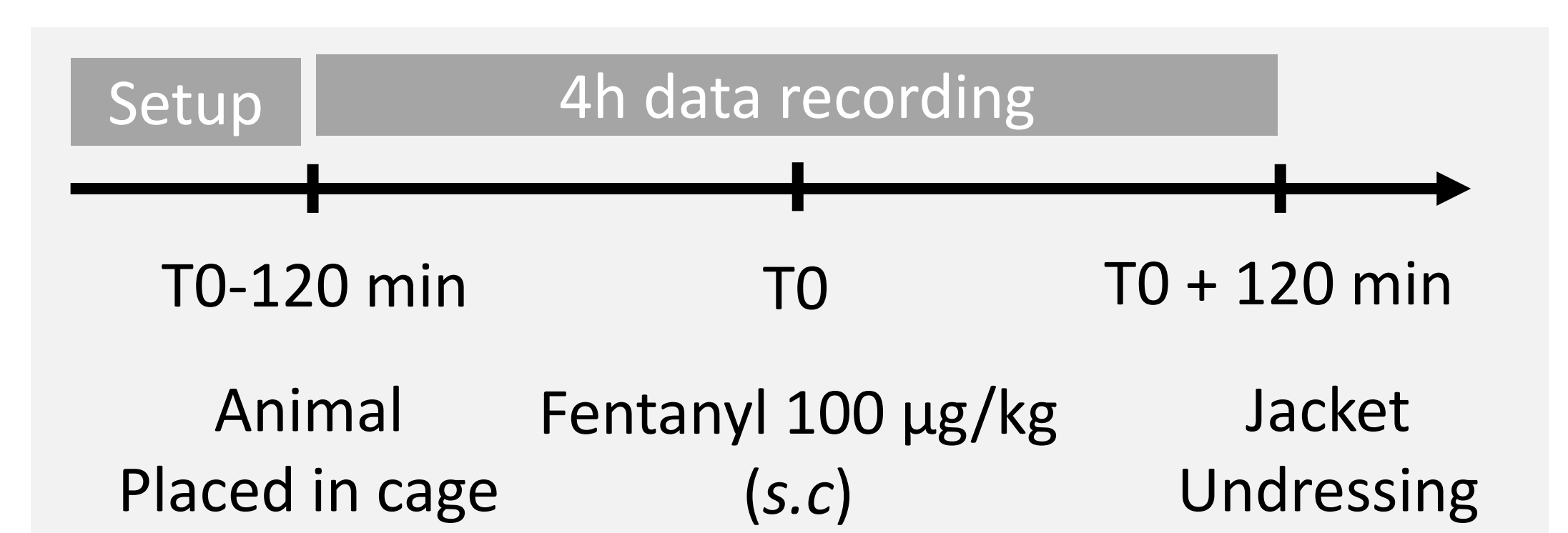
(Table 1) Recorded parameters expressed as mean±sem (relative variation to pre-dose values) . \* Relative time to dosing. Averaging calculated on 30min windows taken after the time indicated.

## Conclusions

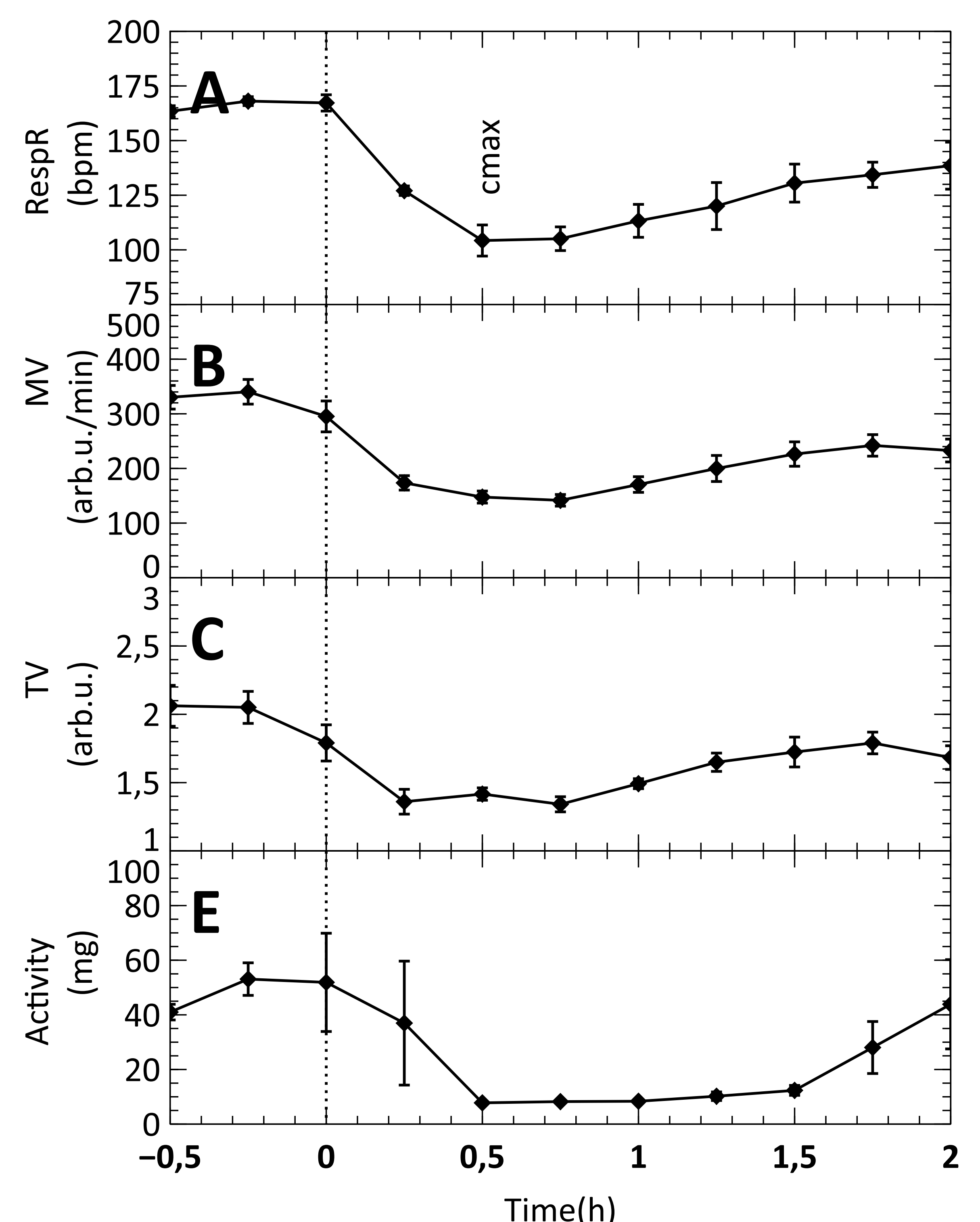
- The DECRO connected jacket permitted to easily quantify fentanyl-induced respiratory depression in a non invasive manner in freely-moving animals.
- This non-invasive jacketed telemetry system can be used to evaluate the respiratory depression for new opioid analgesics



(Fig.1) An Animal equipped with DECRO jacket, Ag/AgCl electrodes are stuck on a clipped area (under the jacket) and a Bluetooth electronic transmitter connected to the sensors is placed into the backpack



(Fig.2) Chronogram of the experimental procedure



(Fig.3) Recorded respiratory and activity parameters evolution represented as average ±sem relative to dosing (dotted line). Average is calculated on 15 min windows taken after the time indicated.

## References

- [1] Flénet T, Fontcave-Jallon J, Guméry P-Y, et al. High-resolution respiratory inductive plethysmography in rats: validation in anesthetized conditions. *Physiol Meas.* 2017;38(7):1362-1372.
- [2] Flenet T, Barret H, Chastel E, Abdel M, Eynard C, Boixel C. Assessment of cardiorespiratory function using telemetric jacket in rodents. In: *SPS 2019, Journal of Pharmacological and Toxicological Methods.* Vol 105. Barcelona: Elsevier; 2019:106824.
- [3] Fares R, Boire A, Eynard C, Flenet T. Simultaneous non-invasive telemetric electrocardiogram and respiratory measurement with a connected jacket (DECRO system) in rats. *Protoc Exch.* 2020.

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