- Ejaculation is a stage into the male sexual cycle, consisting of synchronized and successive physiological events, that form two distinct phases: emission and expulsion. Ejaculation is mediated by neurological and hormonal pathways. Any interference with these pathways may cause ejaculatory disorders, among them, premature ejaculation (PE) which is the most prevalent sexual dysfunction in men.
- Serotonin and dopamine are among the main neurotransmitters that are well-described to be involved in the ejaculation process, whether in human or in rat. Thus, in anaesthetized rat, a complete ejaculatory response is induced by systemic administration of one of the two compounds:
    - **Para-chloroamphetamine (PCA):** an amphetamine derivative that induces catecholamines and serotonin release from monoaminergic nerve terminals.
    - **7-Hydroxy-2-(di-n-propylamino)tetralin (7-OH-DPAT):** a selective D3 dopamine receptor agonist
- In anaesthetized rat, pharmacologically-induced ejaculation model is useful for a first proof of concept of a new potential drug to treat PE, or for the detection of drug affecting the ejaculatory process. In ejaculation disorders area, pharmacologically-induced ejaculation model has a predictive value in human, and thus ideal for screening a new drug candidate for PE.
- Physiological markers of the 2 ejaculation phases can be investigated and recorded during the evaluation period:
    - Seminal vesicle pressure (SVP) for the emission phase, knowing that seminal vesicle secretions represent 50-80% of the total ejaculate volume
    - Bulbospongiosus muscles (BS) contractile activity for the expulsion phase.

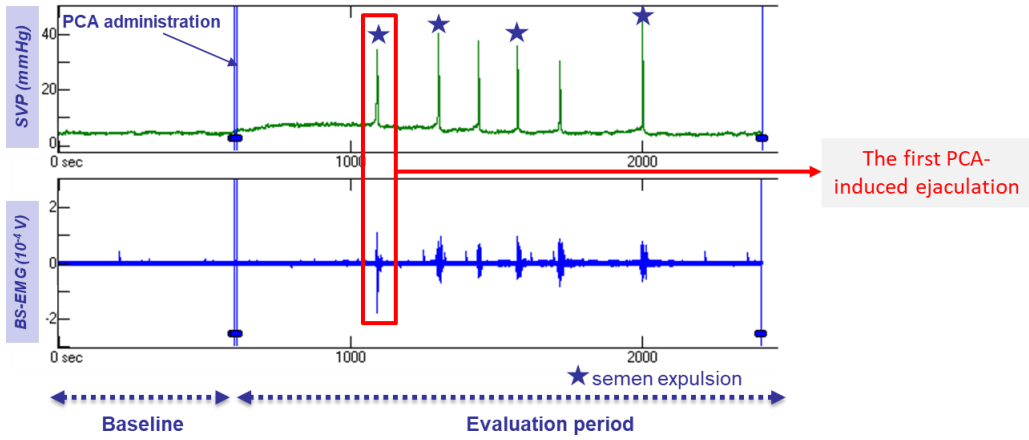

Figure 1: illustration of seminal vesicle pressure (SVP) and bulbospongiosus muscles (BS) activity recordings following intravenous PCA administration in anaesthetized rats (Pelvipharm internal data).

- Behavioral studies can be performed either in non-categorized or categorized rat, categorization being performed using mating tests.
- From standardized mating tests with sexually receptive female rats conducted in our laboratory, the number of ejaculations was found to follow a Gaussian distribution (figure 2). Thus, a sub-group of rats displays a short latency of ejaculation, thereby modelizing premature ejaculation.

Endpoints

- Proportion of ejaculating-rats and latency of their (first) ejaculation (corresponding to the expulsion of a seminal plug)
- Characterisation of SVP increases (amplitude, latency, etc…)
- Characterisation of BS contractions (latency, frequency etc…)

Related Pelvipharm bibliography:

Clément P *et al.* **J Androl** (2006):27:381-389
Clément P *et al.* **Neuroscience** (2007):145:605-610
Kitrey ND *et al.* **Neuroscience** (2007):149:636-641
Clément P *et al.* **Br J Pharmacol** (2008):154:1150-1159
Clément P *et al.* **J Sex Med** (2009):6:126-134
Clément P *et al.* **J Sex Med** (2009):6:980-988

NB: Pelvipharm will gladly study the feasibility to fit this experimental model to its client's needs.