Implementation of non-invasive cardiorespiratory and activity assessment in the juvenile minipig using the Decro® jacket system

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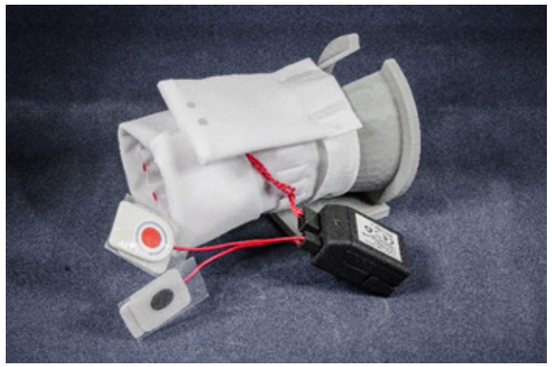
In nonclinical research, animal welfare is the cornerstone of relevant, high-quality data. As invasive technologies that affect an animal's well-being can compromise research results, we have worked to develop alternative methods for collecting data that address both ethical and scientific concerns.

Introduction

Etisense, a biomedical engineering firm based in Lyon, France, has developed a solution for the collection of nonclinical cardiorespiratory data on animal models using the DECRO® system (Picture 1), a noninvasive jacket that uses Bluetooth Low Energy® technology for signal transmission. Looking to expand its applications beyond rats, Etisense has partnered with Charles River scientists to develop a solution that allows the monitoring of cardiorespiratory signals and activity levels of juvenile minipigs.

Göttingen Minipigs have now become widely accepted as a non-rodent species for safety testing, including juvenile animal studies, due to the availability of the purpose bred specific pathogen free breed in both the US and Europe and its physiological similarities with human. The minipig has many advantages over other usual laboratory species such as a relatively large litter size, rapid growth rate, and rapid achievement of sexual maturity. Moreover, piglets can be used for laboratory procedures from a very early age, even from postnatal day (PND) 1 onwards due to a high degree of autonomy shortly after birth. In the work presented here, a non-invasive cardiorespiratory and activity assessment in the neonate juvenile minipig, using Decro® jacket, from as early as the first week of life is described.



Picture 1
DECRO® jacket system.

Method

One litter of seven newborn Göttingen Minipigs (pregnant sow supplied from Ellegaard Research Foundation) was allocated to 2 groups, one group of untreated animals and the other group receiving baclofen by oral gavage, a reference item known to decrease respiratory rate. Piglets were fitted with the DECRO® jacket on the day before treatment (where applicable) for training / baseline measurements, and up to 20 hours after treatment (where applicable). The jackets were setup to simultaneously record three biosignals, namely electrocardiogram, respiration by inductance plethysmography (RIP bands) and activity levels by accelerometry. Proprietary Etisense software with advanced algorithms was used to automatically detect cardiac and respiratory cycles and calculate standard ECG, respiratory and activity parameters. Recording was performed once weekly from 1 to 4 weeks of age.

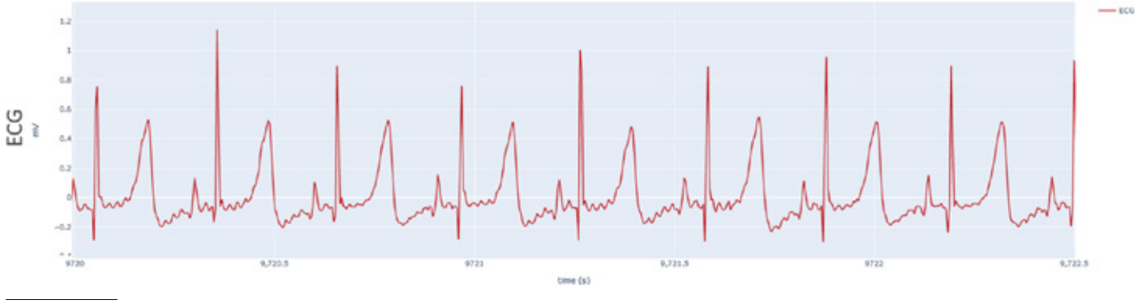


Figure 1
ECG waves in the first week of life, recorded at rest

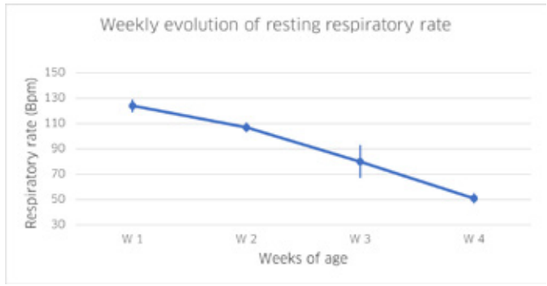


Figure 2
Weekly evolution of resting respiratory rate. Over the first four weeks of life, mean respiratory rates decreased with age.

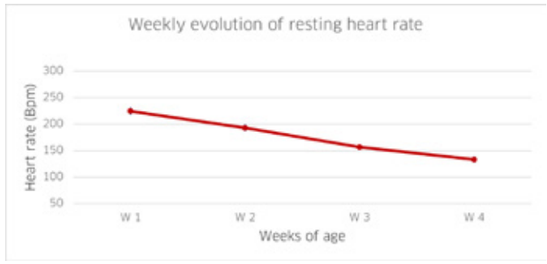


Figure 3
Weekly evolution of resting heart rate. Over the first four weeks of life, mean heart rates decreased with age.

Results

Baclofen-related effect

Based on preliminary internal data and literature, baclofen was tested at 2, 3 or 4 mg/kg, depending on the animals' age and reaction to previous doses. At these doses, piglets showed either reversible clinical signs (labored breathing and decreased activity) or no signs at all, depending on the age at the time of dosing. Baclofen-related effect on cardiorespiratory and activity parameters was only noted at high doses when marked clinical signs were observed (low activity levels and low heart rate and respiratory rate values).

Jacket tolerance and integrity

The minipig-designed jacket induced skin lesions / abrasions in the axillary and cervical areas of all animals. Topical care (ointment application) was applied and the jacket was subsequently modified to ensure better protection by the addition of foam and reshaping of the collar. Despite any potential discomfort generated by wearing the jacket for approximately two days per week for four weeks, no impact on growth (body weights) was noted.

The jackets remained in place for the majority of piglets aged one week and RIP bands embedded into jackets remained operational. The ECG electrodes were occasionally re-positioned but in most instances, the biosignals were recorded as scheduled. From two weeks of age, the biosignals were recorded for all animals but the jackets remained in place and RIB bands operational during the entire recording period for approximately half of them.

Cardiorespiratory and activity analysis

In the first week of age, a clear correlation was found between high activity levels and elevated heart rate (HR) and respiratory rate (RR) values. On average, animals spent approximately 20% of the time resting (defined as activity level < 50mG).

Overall, 90% of ECG signals were of good quality, with well-defined waveforms and low noise, allowing for a proper detection of ECG complexes and corresponding waves (Figure 1). Optimal fitting of the jackets embedding the RIP bands provided good respiratory signals suitable for analysis. At two weeks of age, respiratory rate (90-135 breaths/min) and heart rate (181-252 beats/min) values were comparable with those obtained in a previous juvenile minipig study with animals restrained in adapted slings. Over the first four weeks of life, respiratory and heart rates decreased with age (Figure 2 and Figure 3).

Conclusion

In conclusion, simultaneous non-invasive recording of quality electrocardiographic, respiratory and activity signals and subsequent analyses were achieved in the juvenile Göttingen Minipig using the jacketed Decro® system from the first week of life. Fitting juvenile animals with this device at different post-natal ages had no impact on their growth and behavior. Cardiorespiratory parameters obtained using the Decro® jacket were comparable with results obtained from restrained animals in previous studies (snapshot ECG and visual assessment of respiratory rate). Improvements in both the robustness and comfort of the jacket and recording system are currently ongoing to ensure that uninterrupted data can be obtained from the fast-growing juvenile minipigs through to an age when traditional methodology can be applied.

MORE INFORMATION

ETISENSE website:
etisense.com
The DECRO® jacket:
decro.fr

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