Characterisation of Spontaneous Activity in the Different Zones of the Human Prostate Gland

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Introduction
All men show characteristics of benign prostatic hyperplasia (BPH) upon ageing; the most common neoplasm in men. Lower urinary tract symptoms (LUTS) include increased hesitancy, urgency, frequency and strain, severely affecting the quality of life of men with BPH. These LUTS are exacerbated by an increase in prostatic smooth muscle tone, a major component associated in BPH. BPH occurs in the (1) transition zone of the prostate gland, as opposed to the (2) peripheral zone where prostate cancer occurs (see Fig. 1). However, the aetiology of BPH remains poorly understood, and the fundamental reason why there is an increase in smooth muscle tone in the transition zone remains unknown.

Hypothesis
Our overall hypothesis is that changes in the mechanisms regulating spontaneous activity of the prostate gland, significantly increase prostatic smooth muscle tone and contribute to the pathogenesis of BPH.

Objectives
• To characterise the spontaneous contractile activity in prostate specimens from 20 men.
• To compare the spontaneous contractile activity in the transition and peripheral zone from 8 men.

Methods
Prostate tissue was obtained from consenting patients undergoing radical prostatectomy, and placed into ice-cold RPMI medium supplemented with 5% fetal calf serum and antibiotics (penicillin at 300 units/ml, streptomycin at 300 μg/ml and amphotericin at 1 μg/ml).

A resected benign transition zone (TZ) and peripheral zone (PZ) specimen (10 mm x 15 mm) was collected, with original tissue undergoing radical prostatectomy, and placed into ice-cold RPMI medium supplemented with 5% fetal calf serum and antibiotics (penicillin at 300 units/ml, streptomycin at 300 μg/ml and amphotericin at 1 μg/ml).

Subsequent recordings were made from prostatic preparations (3 mm x 10 mm) using conventional tension recording experiments (Dey A et al, 2010).

Resting Basal Tension vs. Peripheral Zone

Results – Transition Zone vs. Peripheral Zone

Figure 1. The different zones of the human prostate gland. Figure modified from (Giles LG, 2010).

We have previously demonstrated that changes in spontaneous electrical activity with age promote an increase in prostatic tone and contractility in the guinea pig prostate gland (Dey A et al, 2009, Dey A et al, 2010). These spontaneous contractions are likely to be involved in a housekeeping function, and regulate the resting smooth muscle tone of the prostate gland. However, relatively little is known about spontaneous activity in the human prostate gland.

Figure 2. The parameters measured include resting basal tension (mN), amplitude of contractions normalised for weight (N g⁻¹), duration (s) and frequency of contractions (min⁻¹).

Figure 3. An increased resting basal tension in the TZ, in comparison to the PZ, demonstrates an increased smooth muscle tone in the region where BPH occurs. Measuring the different parameters that contribute to spontaneous contractions, demonstrate that there are significant differences in contractility profiles for both TZ and PZ. Spontaneous contractions in the TZ are significantly less frequent (P < 0.01; Student’s paired t-test), longer in duration (P < 0.05; Student’s paired t-test), and half the amplitude (P < 0.05; Student’s paired t-test), in comparison to matched PZ specimens from the same human prostate gland.

Figure 4. Application of tetrodotoxin (n=5), a neural propagation blocker, had no significant effects on amplitude and frequency of spontaneous contractions in the TZ, but significantly lowered the basal tension in comparison to the PZ in this model, and this is the region associated with an increased smooth muscle tone and where BPH occurs. The effects of neural propagation and transmission blockers suggest zone-specific differences in the regulation of spontaneous activity in the TZ and PZ.

Figure 5. Application of amantadine (n=5), an α₂ adrenoceptor blocker, had no significant effects on amplitude and frequency of spontaneous contractions in the TZ (P > 0.05; Student’s paired t-test). This suggests that the regulation of spontaneous contractions in the PZ of the human prostate gland may be different to the TZ.

Figure 6. Application of tetrodotoxin (n=5), a neural propagation blocker, had no significant effects on amplitude and frequency of spontaneous contractions in the TZ, but significantly lowered the basal tension in the PZ (P < 0.05; Student’s paired t-test). This suggests that the regulation of spontaneous contractions in the PZ of the human prostate gland may be different to the TZ.

Conclusions
The TZ of the human prostate gland has an increased resting basal tension in comparison to the PZ in this model, and this is the region associated with an increased smooth muscle tone and where BPH occurs. The effects of neural propagation and transmission blockers suggest zone-specific differences in the regulation of spontaneous activity in the TZ and PZ.

This model provides novel opportunities into understanding the basic physiology of the human prostate gland and the changes that occur, the effectiveness of current and emerging pharmacotherapies directly on human prostatic smooth muscle tone, and may identify alternative approaches to treat BPH.

References

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