Original article

Non-linearity, a dilemma and opportunity for clinical research in urogynecology

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Abstract: The female pelvic floor contains the most complex interconnected nonlinear controlled system of muscles and ligaments in the body. *The dilemma*. Much of the research in urogynecology today is reductionist, never ending classifications attempting to fit complex issues into simplistic reductionist boxes. Examples are the POPQ system, urodynamics, replacing symptoms with numbers, "scores". Use of simple language is suggested to report results and application of Occam's Razor to distinguish relevance of rival systems. *The opportunity*. Complexity and Chaos are the key to understanding the variance inherent in pelvic floor function and are a rich direction for future research. The importance of 'criticality' in speedily changing the bladder phase from 'closed' to 'open' is described as are the non-linear mechanisms driving this system, an external striated muscle mechanism acting against suspensory ligaments, and the internal resistance to urine flow which is proportional to the 5th power of the change in urethral radius by this mechanism. The impossibility of pre-operatively determining the initial conditions as a guide to therapy is discussed and how this can be bypassed by repairing the ultimate cause of the dysfunction, damaged ligaments, with tensioned slings. Repairing the ligaments works by reversing the non-linear cascade of events consequent upon inability of the musculoelastic control mechanisms to 'grip' on the loose ligaments. A simple research protocol for reversing these complex cascades is detailed, by supporting various suspensory ligaments.

Key words: Urogynecology; Complexity; Chaos; Pelvic floor; Non-linear mechanisms.

GLOSSARY

Chaos is the generation of complicated, aperiodic, seemingly random behaviour from the iteration of a simple rule. In urogynecology it applies especially to the feedback systems inherent in control of continence, the micturition and defecation reflexes.

Complexity is the generation of rich, collective dynamical behaviour from simple interactions between large numbers of subunits.

Criticality. A system is critical if its state changes dramatically given some small input. A good example is the almost instantaneous activation of bladder/urethral closure and micturition.

Dynamical system – a set of interacting and interrelated elements that can change in time. The pelvic floor is a classical example, with all structures, muscles, nerves, connective tissues, blood vessels acting co-ordinatedly to achieve organ support, opening and closure.

Integral Theory (IT). States that POP and pelvic floor symptoms mainly derive from laxity in the vagina or its supporting ligaments because of altered collagen/elastin.

Integral Theory System (ITS) or Integral System. A management system based on IT which diagnoses and treats lax vagina/ligaments using squatting based exercises or small strips of tape accurately applied to damaged ligaments.

Linear system is simple and predictive. It is the sum of its parts. 1+1 always = 2.

Nonlinear system: a nonlinear system in contrast to a linear system, is a system in which the output is not directly proportional to the input. Non-linear systems dominate the pelvic floor.

QOL Quality of life.

Reductionism is the practice of simplifying a complex idea to the point of minimizing, obscuring, or distorting it. Examples are new terminologies such as POPQ, urodynamics, some classifications, symptom scores, really, any artificial structure imposed on a Natural system.

VAS Visual analogue scale.

THE DILEMMA

Pelvic floor function is non-linear and therefore constantly variable. Marcus Aurelius, the Roman emperor and stoic philosopher described the holistic non-linear character of Nature thus [1]: "constantly regard the universe as one living being, having one substance and one soul; and observe how all things have reference to one perception, the perception of this one living being; and how all things act with one movement; and how all things are the cooperating causes of all things which exist; observe too the continuous spinning of the thread and the contexture of the web.[1] This quote beautifully encapsulates the modern science of Complexity,[2] that Nature works in an interconnected, holistic and non–linear way: every part of a system affects every other part, with the sum being greater than the parts. Though the pelvic floor contains the most complex interconnected system of muscles and ligaments in the body, very little has been written about the non–linear control mechanisms of these dynamical systems and how they impact on clinical and research urogynecology. Yet much of the research in urogynecology today is reductionist, never ending classifications attempting to fit complex issues into simplistic reductionist boxes. Such reductionism cannot encompass the wide variance seen in clinical conditions and symptoms, even within the same patient (Figure 1).

Karl Popper, discussing the problems of artificial model languages, stated: "thus the method of constructing artificial model languages is incapable of tackling the problems of the growth of our knowledge"; and "It is a result of their poverty that they yield only the most crude and the most misleading model of the growth of knowledge - the model of an accumulating heap of observation statements".[3]

Two such examples are the POPQ system[4] and the predictive value of urodynamics.[5] Replacing symptoms with numbers, "scores", is another example of an "artificial model language".[4] Reporting the change in the total number of episodes of frequency, urge incontinence,

nocturia in a cohort[6] using standard ICS definitions is much easier to understand than a set of numbers. Furthermore symptoms are experienced differently by different patients and the QOL varies considerably even within the same patient (Figure 1). This is the dilemma. Classifications have to be productive and helpful in patient management. Non-productive classifications serve only to burden clinical practice and research.

Occam's Razor - A tool to resolve the dilemma

Occam or Ockham, a14th century English philosopher stated that a simpler solution was more likely to be the most valid, and simpler theories are preferable to more complex ones because they are better testable and falsifiable. In urogynecology this could mean that we should use the halfway system instead of POPQ; the sign of USI instead of urodynamics; reporting the change in the total number of frequency, urge incontinence, nocturia episodes in a cohort instead of a set of numbers.

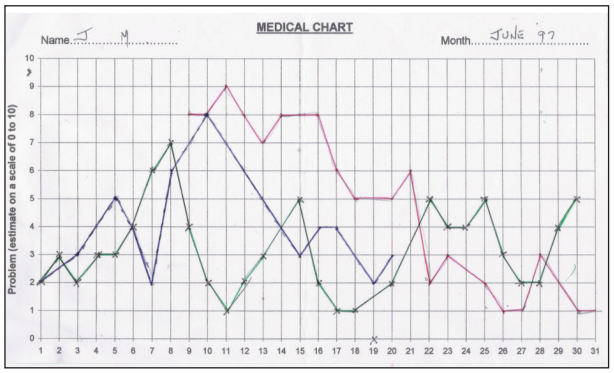

Figure 1. - This graph was constructed from a QOL which used a VAS score recorded on a daily basis by a patient who had urinary incontinence. The non-linearity of the VAS scores displayed question the validity of "Pelvic Floor Scores" and "validations" as performed today. Different colours denote different months. Looking at the top (red) graph, there would be an enormous difference in score depending on whether the assessment was on Day 11, or Day 26.

THE OPPORTUNITY

Complexity and **Chaos** are the key to understanding the variance inherent in pelvic floor function and are a rich direction for future research. Complex and chaotic systems are nonlinear and sensitive to initial conditions. A system is 'critical' if its phase state changes dramatically with some small input.[2] The bladder has two phases, open and closed. The bladder is always "en garde", ready to instantly open (evacuate) or close (continence) depending on circumstance. Criticality is important for rapid phase change. What makes a rapid phase transition possible is

1. The external striated muscle vectors, arrows (Figure 2) which can rapidly open or close the urethral tube.
2. The exponential relationship (5th power) between the radius and the resistance to urine flow[7] which exponentially accelerates 1.

For example, a sudden halving of the urethral diameter 'D' by vector closure (Figure 2) increases resistance by a factor of 32. Doubling 'D', by the vectors stretching the urethra posteriorly enables micturition by reducing resistance to flow by a factor of 32.[7] It is this mechanism which gives instant commencement of urination and instant stoppage of flow.

Continence. Effort such as coughing activates the fast-twitch forward vectors to contract against the suspensory ligaments. This small change in initial conditions sets forth a cascade of events in associated subsystems, muscles (arrows), stretch receptors, suspensory ligaments and all their components, collagen, elastin, nerves, blood vessels. The effect is to exponentially narrow the urethra for closure.

Emptying At a critical point, the hydrostatic pressure of the urine stimulates the bladder base stretch receptors to set off a different cascade of events in the same subsystems to swing the system into open phase, micturition. The posterior urethral wall is stretched open by the vectors (Figure 2) exponentially decreasing the internal resistance; the bladder contracts and empties.

Urgency & Frequency. Any loose ligament will prevent the vectors from stretching the vaginal membrane sufficiently to support the bladder base stretch receptors. Depending on their sensitivity, they may fire off at a low bladder volume to cause urgency and frequency and at night, nocturia. The control of urgency is consistent with a classic chaotic feedback mechanism.[8] This mechanism adequately explains the instability curve of urodynamics and bladder stability in the normal patient during filling; a low compliance bladder is consistent with a partly activated but controlled micturition reflex.[8]

How to address non-linearity in clinical situations?

From a Complexity perspective, the exponential nature of the control system makes it difficult for any system to predict an outcome, as it requires the initial state of the system to be described with perfect accuracy, a nearly impossible task.[2] So any pre-operative test (e.g., urodynamics) is doomed to fail as a predictor. The ITS bypasses this problem by repairing the ultimate cause of the dysfunction cascade, damaged ligaments, with "micro' tensioned slings.[9]

New research directions

The ligament concept of function and dysfunction provides many opportunities for research. It can be tested without surgery by examining a patient with a full bladder. Upward pressure on one side of the urethra

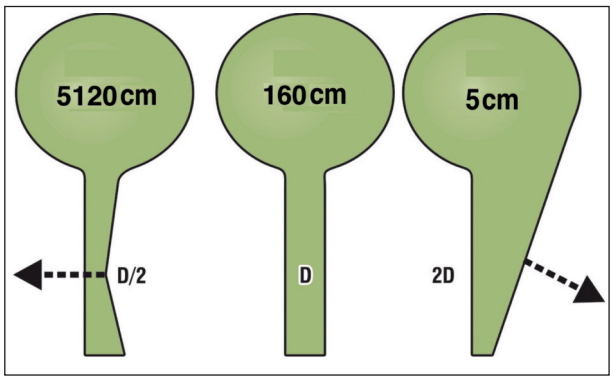

Figure 2. - The non-linear relationship of urethral resistance to continence and micturition (for non-laminar flow). Resting closed (middle figure). 160cm H2O is a nominal pressure for leakage at diameter D. For closure (continence) (left figure). If the forward vector can close the diameter to D/2, resistance to flow increases by the 5th power. The head of pressure required for leakage increases to 5120cm H2O (The inverse of ½: 2x2x2x2x2=32). For opening (micturition) (right figure) If the backward vectors can open the diameter to 2D, resistance to flow decreases by the 5th power. The head of pressure required for leakage decreases to 5cm H2O.

immediately behind the symphysis will control USI and often urgency. A large tampon in the posterior fornix will support the posterior ligaments and often diminish urgency, pelvic pain and nocturia.[9] Gentle digital support of the vagina just anterior to the cervix may diminish urge symptoms and may alter DO (detrusor overactivity).[8] Performed under urodynamic or ultrasound control, these 'simulated operations' would constitute a most original research project. They work by reversing the non-linear cascade of events consequent upon disturbance of the musculoelastic control mechanisms.[8,10,11]

CONCLUSIONS

Non-linearity and chaotically influenced feedback mechanisms are fundamental to Nature. They are the key to understanding the complexity of pelvic floor anatomy and function, day to day symptom variation in an individual patient. They help us make sense of anomalous and varied experimental results, and even to appreciate how the randomness of initial experimental results may influence a whole new direction in surgery in a positive or negative way.

REFERENCES

1. Translated by George Long http://classics.mit.edu/ Antoninus/ meditations.4.four.html (accessed April 21, 2014).
2. Rickles D, Hawe P, Shiell A. A simple guide to chaos and complexity J Epidemiol Community Health 2007; 61:933-937. doi: 10.1136/jech.2006.054254.
3. Popper KR. A survey of some fundamental problems. 0n the problem of a theory of scientific method. Theories. Falsifiability. The problem of the empirical basis. Degrees of testibility. Simplicity. The Logic of Scientific Discovery. 1980; Unwin, Hyman, London, 27-146.
4. Riss P, Dwyer PL. The POP-Q classification system: looking back and looking forward. Int Urogynecol J, 2014; 25:439-440; DOI 10.1007/s00192-013-2311-8.
5. Glazener CMA, Lapidan MC. Urodynamic investigations for the management of urinary incontinence in children and adults. Cochrane Review; 2006; The Cochrane Library, Issue 1.
6. Petros PE. New ambulatory surgical methods using an anatomical classification of urinary dysfunction improve stress, urge, and abnormal emptying. Int J Urogynecology, 1997; 8: 270-278.
7. Bush MB, Petros PEP, Barrett- Lennard BR On the flow through the human urethra. Biomechanics 1997; 30: 967-969.
8. Petros PE Detrusor instability and low compliance may represent different levels of disturbance in peripheral feedback control of the micturition reflex. Neurourol and Urod. 1999; 18:81-91.
9. Petros PEP, Ch4 Surgery according to the Integral Theory, in The Female Pelvic Floor, Petros PEP, Springer Heidelberg 3rd Ed 2010, 157-211.
10. Petros PE, Von Konsky B Anchoring the midurethra restores bladder neck anatomy and continence. Lancet, 1999; 354: 9193: 997-998.
11. Petros PE Changes in bladder neck geometry and closure pressure following midurethral anchoring suggest a musculoelastic mechanism activates closure. Neurourol. and Urodynamics, 2003; 22:191-197.

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