EDITORIAL

Some thoughts on the effect of non–linearity on innovation in urological surgery

Peter Petros[1], Florian Wagenlehner[2], Przemysław Waliszewski[3]

[1]Academic Dept of Surgery, St Vincent's Hospital Clinical School, Sydney, Australia
[2]Clinic of Urology, Pediatric Urology and Andrology, Justus–Liebig–University, Giessen, Germany
[3]Department of Urology, Pediatric Urology and Andrology, Justus–Liebig–University, Giessen, Germany

TERMS AND DEFINITIONS

Chaos theory is a set of concepts which studies the behaviour of dynamical systems that are highly sensitive to initial conditions.
Deduction. A form of reasoning which works from the more general to the more specific. Deduction is a tool for rigorously testing a hypothesis.
Dynamical system – a set of interacting and interrelated elements that can change in time.
Induction. A form of reasoning whereby general propositions are derived from specific examples. Induction is when an observation leads to a hypothesis.
Integral Theory (IT). States that POP and pelvic floor symptoms mainly derive from laxity in the vagina or its supporting ligaments.
Integral Theory System(ITS) or Integral System. A management system based on IT which diagnoses and treats lax vagina/ligaments in 3 zones of the vagina.
Non–linearity. A system whose output is not directly proportional to its input.
Posterior fornix syndrome. A system complex comprising urgency, nocturia, abnormal emptying and low dragging pelvic pain caused by laxity in the uterosacral ligaments.
Reductionism the practice of simplifying a comp lex idea to the point of minimizing, obscuring, or distorting it.
Urinary stress incontinence (USI) urine loss on effort.

AIM OF THIS EDITORIAL

The aim of this editorial is to introduce the concept of non–linearity (complexity) and to present a few thoughts on its impact on innovation in surgery. Some of the steps involved in the discovery of the midurethral sling and Integral Theory System are provided as examples.

INTRODUCTION

Nature works in an interconnected, holistic and non–linear way: every part of a system affects another part and also, the system itself. Yet very little is written about non–linearity in medicine or research medicine in mainstream journals.
One famous description as to how Nature works was written by Marcus Aurelius, the Roman Emperor and Stoic philosopher [1].
Always think of the Universe as one living organism, with a single substance, and a single soul; and observe how all things are submitted to the single perceptivity of this one whole; all are moved by its single impulse, and all play their part in the causation of every event that happens. Remark the intricacy of the skein, and the complexity of the web.
This description emphasizes one fundamental scientific fact: Medicine, like Nature, consists of complex nonlinear systems operating in every part of the body. These systems are balanced and interact with each other. A pure reductionist approach, therefore, has little place in the study of such a system, as it is literally impossible to isolate just one single factor unrelated to anything else. One has to look at the whole picture.
One example of this is the practice of using single urodynamic flow rate values in articles on "obstructed" micturition. The flow of urine through the urethra is non–linear in that it is inversely related to the 5th power of the radius [2] for non–laminar flow (doubling the radius increases the resistance to urine flow by a factor of 32); the urethral tube is opened (and closed) by an external striated muscle mechanism reliant on intact suspensory ligaments, so even the slightest difference in tissue tension or timing is exponentially magnified to the 5th power, ensuring that flow rate can never be adequately reproducible

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[3] he same criticism applies against drawing conclusions from single pressure values of "detrusor overactivity" ("DO") obtained during urodynamic testing; the instantaneous "DO" pressure recorded ultimately reflects the instantaneous urethral radius and therefore resistance, a resultant of the interplay of the natural urethral closure mechanisms which close the urethral tube [3] and the micturition reflex which opens it out [2]. The characteristic sinuous curve characteristic of "DO" is consistent with the slight time delay taken to switch from domination of the closure reflex (raised urethral pressure) to domination of the micturition reflex (fall in urethral pressure). "DO" as applied today is reductionist, in that it takes a single reading from an exponentially determined dynamic process and draws important conclusions, for instance, in a patient with mixed incontinence, whether to operate or not.

First steps in innovation – towards a hypothesis

The first step is for an "innovative" scientist is to "discover" how it works, then to apply that knowledge in solving a difficult clinical problem. Popper [4] describes two mechanisms, induction and deduction. Induction, simplistically, takes an idea or observation towards a hypothesis. The hypothesis then has to be tested in a valid way, by deductive experimentation: "if "a" is so, then "b" follows. In 1986, the 1st author, PP, noted a dense collagenous tissue reaction to implanted Teflon tape. PP had previously noted that pressing a hemostat directly upwards immediately behind the pubic bone controlled urine loss on coughing (USI). Two hypotheses were formed,
The cause of USI is a loose pubourethral ligament (PUL).
Implantation of a tape will reinforce the damaged PUL by creating an artificial collagenous neoligament.
How non–linearity (randomness) may inadvertently affect research directions
PP obtained permission from the hospital IRB to perform two prototype midurethral sling operations in 1986. Both worked immediately, the patients passed urine immediately, went home the same day and were continent 10 years later. However, when a systematic study was commenced a year later, results in the 1st case series showed only a 50% cure rate. On this basis, the probability of achieving 2/2 success in the initial 1986 operations was only 25%. Conversely, there was an equivalent 25% probability of 2/2 failures. If this had occurred, there would be no midurethral sling today. *What this means is that the Innovative Scientist cannot assume the concept is wrong (or correct) on the basis of 2 cases.* One needs some luck and a lot of persistence. Marion Sims, the fistula pioneer, had many attempts at fistula repair before he finally succeeded with silver wire.
Variation Nonlinearity describes variation and Chaos Theory describes the feedback control mechanisms which drive non–linear systems. The challenge is to create a management system which makes allowance for variation and to avoid the rare "Black Swan" events inherent in Chaotically controlled systems. The Integral Theory System (ITS) is to our knowledge, the only management system to date which recognizes variation and nonlinear dynamics in its diagnostic and surgical systems.

Testing the theory on which the Integral System is based

"Organ prolapse, symptoms of stress, urge, abnormal emptying and some types of pelvic pain arise from laxity in the vagina or its suspensory ligaments, a result of altered collagen / elastin" – Integral Theory.

Pubourethral ligament
One part of the Integral System states that pubourethral ligament (PUL) laxity is the principal cause of USI and is also, an important cause of urgency, Figure 1. For the midurethral sling, which reinforces the PUL, this was done in a deductive way [5]. A hypothesis was formed of what each factor contributed, each variable (PUL, suburethral vaginal hammock, external ligament) was tested in turn and the effect was evaluated [5]. Reinforcement of the pubourethral ligaments with a midurethral sling and tightening the suburethral vagina in patients with USI has not so many variables and so was reasonably amenable to a series of deductive experiments, each testing a different variable [5]. Far more complex is how to scientifically evaluate other structures, for example, uterosacral ligament (USL) function.

Uterosacral ligament

Another part of the Integral System states that uterosacral ligament laxity causes "posterior fornix syndrome" symptoms of *urgency, frequency, nocturia, abnormal emptying, pelvic pain,* (Figure 1).

The hypothesis for symptoms arising from USL, according to the Integral System (ITS), is that adequately tensioned uterosacral ligaments provide a firm anchoring point for the muscles which open and close the urethra [3, 6] and supports the nociceptic fibres which run through it [7].

The authors have found that a tensioned TFS (Tissue Fixation System) sling which reinforces the

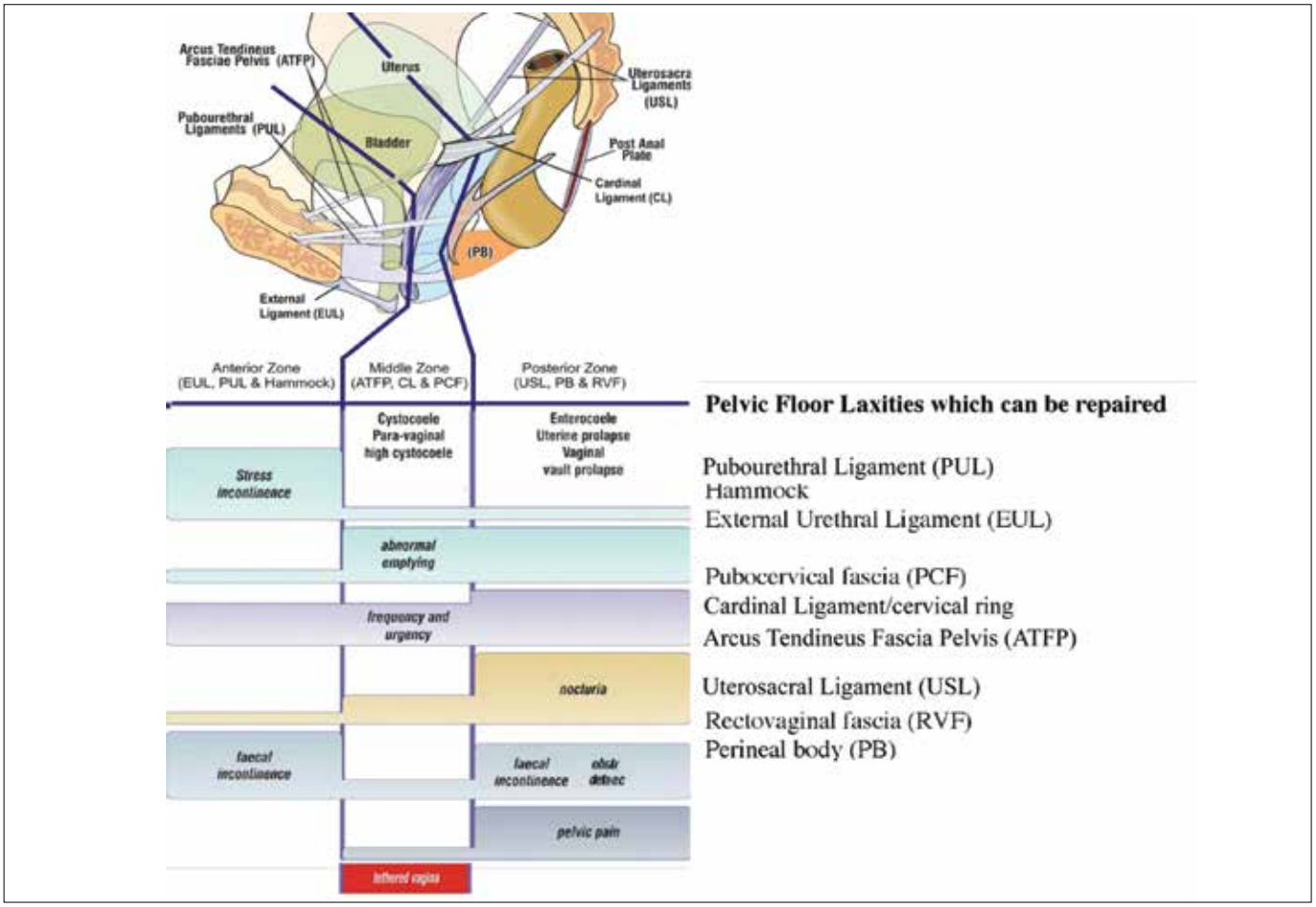

Figure 1. *Diagnostic algorithm uses symptoms to predict zone of damage. Where symptoms such as urgency occur across more than one zone, Figure 1, symptom grouping is used to make the diagnosis. The supporting ligaments/structures naturally divide the vagina into 3 zones: Anterior External meatus to bladder neck, Middle Bladder neck to cervix, Posterior Cervix to perineal body. The height of the bar indicates probability of the symptom originating from damaged structures in that zone. Note that the uterus is supported partly by CL (middle zone) and USL (posterior zone).*

uterosacral ligaments (USL) will variously cure/improve up to 70–85% of "posterior fornix syndrome" symptoms, posterior zone, Figure 1. These results appear to support the hypothesis, but they do not prove it. The proper scientific approach to proof would be to isolate the anatomical factors deemed to influence USL tension (all the pelvic muscles, other connective tissue structures such as cardinal ligaments, rectovaginal fascia, parasympathetic nerves which influence USL contractility etc.) and then test each for its effect on function. Lack of a suitable model aside, the nonlinear variation inherent in USL anatomy [8], plus the greatly varying sensitivity of the nociceptic fibres (pain symptoms) in USL and the stretch receptors at bladder base (urge symptoms) which are also non–linear, render any direct scientific testing impossible.

Management– How the ITS diagnoses and restores ligamentous tension and overactive bladder symptoms

Diagnosis. The Pictorial Diagnostic Algorithm, Figure 1 is a summary guide to diagnosis and management of pelvic floor disorders. It is what Popper would call "a working hypothesis", based on the outcome of the 1st author's extensive surgical experience repairing specific ligaments. It incorporates nonlinearity: the bar size gives an estimate of frequency of occurrence of a symptom in a particular zone.

Non–linear surgical restoration of ligament tension by the TFS

The TFS prosthesis incorporates the patient's own feedback control system in its surgical methodology. Using the one–way system at the base, the tape is tightened

until a resistance is felt. This is a classical application of Gordon's Law [9]: a muscle will contract efficiently only over a defined length. If its insertion point, in this instance, the ligament/ vaginal fascia is loose, the muscle effectively lengthens. As the tape is tightened, it shortens the ligament/vaginal fascial insertion until the muscle contractility returns. This is felt by the surgeon as an increasing resistance to tightening. In this sense, the TFS harnesses the patient's own non–linear control system to assess the tightness required.

Symptomatic improvement following restoration of uterosacral ligament tension by approximation with a No1 Vicryl can be as high as 80–85% for each of the "posterior fornix" symptoms [10, 11] in the 1st instance. By 3–6 months, the tissues begin to loosen again, with increasing failure, hence our introduction of the posterior polypropylene sling [6, 11] to permanently strengthen USL. This is just one example of the complex chaotic dynamical system of bladder/urethral control described by Waliszewski [12] and in a slightly different context, Petros [13]: USL laxity sets in motion a cascade of events resulting in the "posterior fornix symptoms", fig1. Tightening the USLs reverses this cascade, resulting in symptom cure [6, 10, 11].

Waliszewski at al. [13] described the urethra and urinary bladder as a complex dynamical system. Its function was described in a holistic manner by a family of fractal dimensions. All urodynamic curves analyzed in that pilot study [13] possessed fractal structure. That structure has been identified either in the filling phase or in the voiding one by the size–frequency algorithm. It has a cumulative normal distribution profile, and, therefore, can be described by the appropriate power law; the prerequisite condition of the existence of the scale–invariant fractal structure. In some cases of long–lasting obstruction, the urethra–urinary bladder system revealed a tendency towards chaos since one of the holistic parameters, the Hurst coefficient H, reached values greater than 0.5 in the voiding phase.

Certainly, the holistic approach is a way to go in future research on urethra and urinary bladder. In particular, research *in silico* may help to identify the appropriate models, and to test hypotheses [12].

Next steps – a more scientific validation of the Integral System

Given the issue of non–linearity, we see scientific validation of anatomically based management systems such as ITS in the future ultimately as a statistical exercise. A very large data base with many participating surgeons will be required before an accurate percentage incidence can be assigned for a symptom in a particular zone and whether a particular treatment is effective.

It is likely that at some stage an anonymous data base posted on the web by every surgeon performing a procedure may become compulsory. Relevance of the data posted will be a major challenge. Meanwhile, case report series on safety, efficacy, complication rates [5–8, 10, 11], subject though they may be to variation and non–linearity, remain an important method of assessment. Case report series build an accumulated body of knowledge consistent with our 2500 year old medical tradition going back to the time of Hippocrates, as does the understanding of Chaos Theory and non–linearity, as evidenced by Marcus Aurelius's writings [1].

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, anomalous and varied experimental results, even how the randomness of initial experimental results may influence a whole new direction in surgery in a positive or negative way.

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Correspondence
Prof. Peter Petros
pp@kvinno.com