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Reflections, patient's perspective, and theoretical considerations

M. Bouchon

Reflections on observations

A short-term cascade effect:

The short-term observations (table 1, in main article) are consistent with the literature on OT and ADH, except for the near-instantaneous effect. The timing of the non-immediate effects appears consistent with the half-life of OT and ADH, and a cascade of actions, hormonal/systemic and then as neuropeptides in the brain. The effect at 3 minutes, affecting stiffness and stretching pain seems related to OT (which has a 3 minutes half-life) but does not seem to be described in the literature.
Effects at 10-15 minutes seem to reflect ADH (half-life 15-20 minutes) and its vasopressive role in osmosis and extra-cellular swelling, and a possible role of fibroblasts in mucus production and stiffness.
The more lasting effect seems related to the action of ADH on kidneys, an interaction with aldosterone, OT hormonal action on thermogenesis, and neurally mediated vagal stimulation (control of vital and digestive functions, although not all such functions are controllable this way). Mucus effects suggest again a role for the fibroblasts.
Some of these effects also suggest actions on surfaces and fluid-filled bursae in joints, and the neglected role of fibroblasts in producing the 'amorphous ground substance' connective jelly (as opposed to fibrogenesis for constructive granulation and scar tissue, also involved in degenerative fibre concretions).

A cumulative effect with repeated dose:

Once only, the effects above were not achieved, probably because the patient ate high GI carbohydrates (chocolate croissants she calls 'energy food') to help sustain a mental effort. This, she says, 'activates the mind but agitates the brain' and weakens her breathing mechanics. She took a second dose 45 minutes after the first (5am). The overall effect (table 2, in main article) was to counteract symptoms (hypopnea during day and night, deep cold in the spine, and reactive menopausal hot flushes) that occur with activation of the brain's directive role, but also to induce a recognisable cognitive change.
The effect of this repeated dose was to 'reactivate' sufficiently to reduce physiological strain (sense of 'struggle'), and enable spontaneous postural correction. This phenomenon is familiar to the patient, but mostly lost in recent years of increased stress. This physical activation of movement often manifests as yawning, stretching, and repetitive bodily activity. It appears triggered by the autonomic-system, and reduces stress-related, exhausting sympathetic agitation.

A long-term effect: stress-governed, remnant effect after 2 weeks of treatment

This protocol produced a number of longer-lasting improvements (table 3 in main article), small but broad, including in hydration, which lasted for two weeks after the treatment, and then waned. Restarting OT treatment later brought only lesser relief, because stress pressures out of the patient's control increased again, and this strategy was not sufficient to help coping successfully. The complementary societal ability to 'make lifestyle changes' (e.g. more physical activity, get away from sensory, food, and mental stimulation) remains a major

issue over which a family doctor has little control, and the patients often feel the same way. The reactive threshold of sensitivity to stress remained high, as the following shows.

Patient's perspective (1)

"This OT treatment makes it easier simply to be alive every day, and helps me to survive the pressures with less pain. But it does not resolve my sensitivity to stress: beyond a certain point, pain, misery, and the distress of an agitated brain-mind take over. A really useful effect is that, if external pressures do not push me too far, OT reduces drastically the need for the 'energy foods' that I eat to reduce fatigue and perform mental /computer tasks, and it stops all craving for sugar and carbohydrates, fats (brie cheese or ice cream), and the low amounts of dark chocolate I use (all 'energy foods'). Under pressure, the cravings return, even with OT. Inversely, if I eat sugar or dry carbohydrates (for example, tempted by other people's normal diet), I quickly feel dehydrated and swollen, especially the abdomen and face, the OT effect is lost, until the next dose, and I crave even more sugar (very high doses). It is a virtuous cycle that changes direction, and becomes vicious and counter-productive: at first, it is like gaining a second wind, but then it pushes to 'exhausting my reserves' and 'energy hunger'. There is a direct relation. Salt works in the same virtuous/vicious cycle reversal as sugar. Last year, in hospital, I became all swollen from the saline IV. Yet little bit of salt on the tongue can quickly rehydrate me for a short time; but if I take too much, it becomes addictive (seeking salty foods) and brings on pain and catabolic proteinuria in the urine. The reversal and the internal and behavioural effects depend on how much pressure or stress I sustain, and they are also a matter of dose."

Theoretical considerations

These observations raise a number of unanswered questions.
Several organic osmolytes are part of this patient's nutritional program, for reasons related to nervous system, mitochondrial energy, and electrolyte balance: betaine, taurine, inositol, and glycerol. It is conceivable that salt and sugar (also an osmolyte) ingested in large quantity might cause too rapid compensatory reactions in the water metabolism (fast: breathing, slow: kidneys), but at a sub-clinical level rather than critical, causing low-grade but systemic swelling. Beyond the most obvious known behavioural effects of sugar, for example, how does a particular food or drink influence electrolytes, the OT/ADH system, and stress susceptibility or thresholds? Could unaware self-medicating with salt, sugar, drinks, changing food tastes in a normal diet, and the 'nutrition industry' derived mineral-containing 'healing' substances, have a role in self-managing an apparently spontaneous hypothalamic osmostat function coupled with external influences, thus contributing to maintaining 'water balance' under pressures such as stress or physical fitness training? Could this affect sodium in cellular processes and therefore modulate the basic osmosis throughout the body and brain? Effects of large doses are understood, and known to affect mind and behaviour, but little is known of assumed 'normal variations'. In a sensitive patient these small variations have large effects.

Given the current public status regarding diabetes mellitus ('sugar diabetes') and obesity, the growing burden of degenerative diseases and stress-related illness in developed countries, the problems of unmanageable behaviours (un-sane rather than insane, in children, adolescents, and adults alike, or 'sick behaviour' rather than 'disease'), and the mystifying drift effect on children's health worldwide, these are highly relevant questions. A more basic approach might warrant some investigation of the hypothalamic osmostat, its sensitivity threshold, and its 'central' role in brain functions, and in both physical and mental health. Its *systemic physiological* effects might possibly be fundamental to the overall 'healthy' or 'unhealthy' status of the general population, as much as our 'human nature' can be influenced by psycho-social adaptation and mind-processing effects, which can be controlled with specifically targeted drugs or high-dose OT. For the simple purpose of maintaining health in family medicine, it would be useful to go back to acquiring basic *physiological* knowledge (less discriminated and lost in very small details than contemporary medical science tends to produce), relating the roles of OT and ADH to the basic vital functions, in the context of small doses and endogenous normal function. There is little information from current medical research on their physiological interactions with:

-vitamin D, parathyroid hormone, calcium (beyond bone calcium: calcium channels in metabolic and cellular functions, implications for kidney integrity and induced neural cell activity or death), and lipid metabolism;
-other mineral electrolytes (e.g. Ca^{2+} and Mg^{2+}), osmolytes (e.g. sugar, and salt stress), mineral corticoids (as opposed to the more popular glucocorticoids), with implications for metallo-enzymes activation and hormones such as progesterone; (A curious coincidence might turn out significant: a metallic fragment, of unknown origin and composition, is lodged in this patient's head, near sphenoid sinus, noted on a dental X-ray many years ago, but not explained. Such a fragment was also noted in a case report of reset osmostat in a healthy patient [b]);
-nitrogen oxide effects on breathing mechanisms mediated by the brain and cognitive changes (which can be used as indicators, just like emotions or behaviours)
-fibroblasts: they have OT receptors [a] and produce fibrous deposits (which types, under which conditions?), but also the 'ground substance' connective jelly (a very neglected topic), and in relation to gelatinases, other metalloproteases, their inhibitors, and tissue degeneration.

A gap in understanding exists for pain, for diffuse syndromes such as fibromyalgia ('unknown cause', 'not well understood aetiology', not one particular 'cure'…), but also for the role of water in general health. Why is there a drift in the 'normal' reducing water content of the human body from birth to the aged desiccated body? Why is it normal to urinate in the morning, even in a dehydrated body, without drinking at night or kidney dysfunction? What impact does this have on our ability to maintain adaptive health under stress, but also on the vital functions and hypothalamus driven basic behaviours? What is the relationship with the dehydrating the effect of progesterone in some menopausal women?

Inversion

This report also points to gaps in the way we model both stress and osmosis. For example, what makes a brain 'sensitive', and why the stress reaction may not be auto-limiting once stimuli abate, remain open questions. The generally accepted modelling in terms of directed 'activation', of 'up and down' (HPTA axis, and evaluations), does not explain counter-productive effects, such as the vicious/virtuous cycles reversals, and inversed negative effects. An effective or 'virtuous' intervention in many people often results in 'vicious' effects in this patient, and vice versa.

This patient belongs to the first generation of individuals born, in the fifties, by routine birth induction with high-dose OT, and bottle fed. There appears to be no longitudinal studies of the 'oxytocin babies', although the OT/ADH stress response system his known to have lifelong developmental effects [c]. If administered too quickly for birth induction, OT can inverse the effects of the neurotransmitter gaba ('gaba switch'), from calming to stimulating [d]. This patient's speedy birth delivery after induction (just a few minutes), and her current condition, suggest that the high-doses of OT-analogs then used might have altered permanently the operational stability of her hypothalamic osmostat, its threshold of response, and might be implicated in inverted effects and in making her system or her brain a 'sensitive' one. These reflections point to a possible long-term derivation of global effects (including psycho-socio-mental and behavioural, as well as physically systemic: body temperature, sleep, appetite, etc.) that could involve cumulative, time, or dose-related effects.

Subclinical undernutrition syndromes, terminal osmotic dysfunction

— 'water stress' that 'initiates'?

Osmosis-based syndromes are described by thresholds, substance quantities, or functions that are too high or too low, and often relate to critical or terminal illness. Chronic syndromes often involve both highs and lows, in different aspects of the conditions. Stressed patients also mention both, and this patient experiences *variable* thresholds, depending on her 'state'. Polydypsia and polyuria were undiagnosable in this case, because the thirst stimulus and urination patterns fluctuated from one day to the next, but the patient was not free from

these symptoms either. In certain circumstances, could the osmostat not have fluctuating set points? (under which conditions?) Other baffling similarities exist between widespread forms of undernutrition occurring in both chronic syndromes (subclinical) and terminal or geriatric patients (e.g. protein-energy malnutrition – many terms exist for this, in various contexts, including 'wasting'), in secondary malnutrition syndromes such as Kwashiorkor (impacting on lifelong growth), and even with 'hidden hunger' and 'water stress' in plants (drought impairs root nutrition, and the plant's failing 'hydraulic framework' reminds of a slouching human spine). The farmer also recognises in his animals certain 'sick symptoms' due to dehydration or malnutrition (e.g. scruffy hair that falls out or breaks), yet does not see the connection to human health, his own.
Clearly, the high specialisation and fragmentation of current knowledge, and the lack of connection of medical knowledge to animal and plant knowledge, is hiding something that is crucial to maintaining the simple ability to live and remain in a healthy state without undue strain. On the contrary, our frameworks describe the necessity of constantly entraining adaptability to survive, by compensating for both external and internal activity or stress loads, which constitutes a physiological strain not without costs.

Stages, phases, and states

The osmosis-related syndromes listed in the main article often relate to critical conditions or shock. Stress may be viewed as a lower-grade form of 'shock' (think of 'emotional shock', which does not manifest the characteristics of physiological shock). Subclinical signs could denote an even lower-grade form of 'shock' or strain with dangerous long-term effects, despite few objective short-term effects. For example, cerebral salt wasting syndrome is a result of emergency clinical intervention, but shrinking linked to dehydration can be subtly progressive (e.g. brain in ageing, cerebrospinal fluid in spinal degenerations); could salt or osmolytes and dehydration be involved at subclinical level? Chronic syndromes often have 'flare-ups', acute phases often correlated with 'stress levels'. Levels, phases, and stages are terms habitually used to describe shock in critical patients, as well as strain in an undernourished physiology, which is associated with a vague sense of 'doom' in low-grade illness. They are used also for psychologically understood mental processes that relate to distress, social emergency crisis, grief, or culmination of struggle in the 'sick behaviour' that is deemed 'maladaptive' in human sciences — Yet, this is also is a diffuse 'stress syndrome' of physical strain under 'stressed conditions', arising from ongoing physiological compensations that become an established adaptive state with a 'sick' appearance (such as dark circles under the eyes). There are striking similarities, at any degree of recognised gravity, in the 'stages of deployment' of any critical phenomenon ('development' of *both* negative effects and positive or proactive compensations), in other fields than medicine as well. These are often described as changes in morphology, topography, a migrating geography, configuration (deformation, disturbance), etc., or as distortions, which suggests the use of a basic form of topology.

Taking into account all these situations and descriptions leads to complex frameworks of explanation that somehow always yield having to face unexplained or uncontrollable cumulative, time- or dose-related inversions and reversals. For the physician, this brings more complicated testing (also less 'cost-effective'), and even more difficult reasoning to choose a treatment (or simplifying by just prescribing a recommended medical drug). The following suggests a less differentiating but more global approach.

Patient's perspective (2)

"It seemed to me that the effects, irrespective of their medical explanation (or lack of), were 'spreading', from a 'core' located around the base of the head, down to the body along a vertical axis (back and front, not just the spine), then to 'periphery', and then 'back up' to the head. This felt like the brain 'high-jacking' the hormones to 'jack-up higher' both my physical and mental activity, 'activate me', or entraining my 'survival mode'. This has also occurred with the bio-identical progesterone treatment, with energy foods, and in other situations. The mechanism can be endlessly induced again and again, internally or externally, but it has deleterious consequences - those of stress and, in the long run, exhaustion and loosing the ability to adapt. This kind of changing topography and re-initiating is common in my experience."

This 'high-jacking' can be related to the fact that intranasal administration has been shown [c] to pass the blood-brain barrier, and penetrate the central nervous system. This statement suggests a dose-related shift from OT as hormone acting peripherally with systemic effect, to OT as neuro-hormone acting directly on the brain, with central effects, but also an 'integrative' role upon the body and behaviour, as is attributed to some other neurotransmitters (histamine in particular). The brain then governs the body's sub-systems like an orchestrator, with consequences for both extremities (e.g. limb and face swelling and 'bad circulation' in limbs) and core vital functions in many localisations.

The effects observed in this case suggest that OT can be understood globally as inducing *directional* processes (inside-outside cells, brain-body, through surfaces, etc.), and an adaptive/compensatory state (coming in stages or phases) that can become 'driven', over-active, auto-reinforcing. Nevertheless, in some situations as in this case, this 'stress state *initiator*' appears to be also able to *stop* these *physiological* mechanisms before they become counter-productive. (This is consistent with current literature on countering social stress). Such reversal is used in treating shock, for example.

Topographic and timed changes are known in the geographic migration and flaring up of pains or other symptoms in fibromyalgia, and at various biological levels. They suggest topologic properties (topology describes small distortions in shape, and geometries of 'oriented' activity): in this case, surfaces displaying productive flows such as mucus, transports through double-sided surfaces such as osmosis and ions transport across cell membranes, vertical axis of entrainment also fanning out like a tree through the nerves, tensions in sheaths, tendons and ligaments, pressure gradients in fluid mass, etc. Timed cascades and effects related to speed, dose, or localisation (e.g. excitatory/inhibitory in central or peripheral nervous system [e]), or long/short lasting effects [f], have common topologic properties. These can relate them geometrically, and show their connection to inversions, reversals, and counter-productive results. These phenomena are difficult to understand, and are an increasing concern in many specialised fields, in both theory and practice, as well as in medicine, where they are expressed in various but intrinsically similar ways: e.g. 'giving rise to sedation' [g], gaba 'switch' with OT [d], Serotonin 'paradox' [h]. The near-instantaneous effect in this case (table 1 in article, first line) seems impossible to match to explanations using neuroendocrine 'signals' and 'transports', but modelled this way, could be understood as the absence of such 'oriented' movements, or their not being necessary for local functioning.
Processes that switch from auto-limiting to auto-reinforcing are common in physiology and cellular biology, but not clearly modelled at the level of a patient's physical behaviour. One of the striking similarities between all descriptions of 'deployment' into critical states, be they flare-up, syndrome or disease, or other forms in non-medical fields, is that all they display an overall drift (in specific parameters, or globally). In medicine this often involves the 'water balance' and a state of un-met need (nutritional or water status). The various models are often contradictory if taken out of their contexts (which we tend to do routinely).

A simple form of geometric topology [i] can cover all these phenomena generally by describing the 'deployment' or arising of a critical stage, surface 'tearing', or 'holes'. It could relate the medical syndromes more directly to biological function, symptom-sensations in the patient, to the stress elements, and to the basic sense of 'healthy/unhealthy' behaviour or state. It clarify how central sensitivity syndromes arise under pressure, without having to place aetiological causes (that seem so variable and controversial), or having to localise them in a 'system', closed, open, or interactive (which brings definition difficulties). For 'syndrome' patients difficult to diagnose, this might bypass the problem of subclinical observations that do not match 'objective' symptoms or recognised nosology, with associated patient invalidation, and give them access to less drawn-out clinical support (and therefore less costly for both patient and the community). The topologic approach might also offer a new perspective on the limitations we place on the roles of water and the ground substance: amorphous substrate, directional carrier for transport, pressure-gradient governed flows through surfaces, tubes, or holes, etc., and what we may consequently miss. In this case, this approach led to a new treatment idea that did not worsen the general condition or any aspect of it, and did not create discomfort for the patient and lead to non-compliance.

Conclusion

A different framework using a basic form of geometric topology could help understand better the inverted and counter-productive effects, as well as speed or dose-related effects that are found globally in many fields in and outside medicine. It might bring general insight, with less differentiating complexity, into how central sensitivity syndromes, reactive stages, and shock states arise, and why fluids and the influence of the water metabolism are involved in many descriptions of critical, onset, and progressive symptoms (or early and advanced, e.g. effects on circulation, digestion, breathing, posture, sleep, dehydration, swelling…).

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Tables (see main article)

Table 1: Short-term cascade effects of low-dose OT treatment (patient perspective)
Table 2: Cumulative effects of low-dose OT treatment (patient perspective)
Table 3: Long-term effect of low-dose OT treatment: stress-governed and remnant effect after 2 weeks (patient perspective)