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Transient nature of stable behavioural patterns, and how we can respect it☆

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This brief opinion paper suggests continuing ongoing efforts to examine existing and potential theoretical paradigms and formalisms. The paper outlines a need for a shift from implicit behaviourism in neuroscience and psychology to the Functional Constructivism (FC) approach. The paper also discusses the limitation of the view that all behaviour is goal-directed. The FC approach highlights the variability and transient nature of behaviour and its neurochemical biomarkers. It presents behaviour as a generative process in which behavioural products are specialized according to an individual's capacities rather than dictated by universal environmental demands or clear goals. Proper diagnosis of consistent behavioural patterns (CBPs, i.e. temperament traits in healthy individuals and symptoms of psychopathology), therefore, should include analysis of cycles of functional activities that people are involved in. The paper proposes a 12-component classification of psychiatric symptoms and classification of contexts based on the neurochemical model Functional Ensemble of Temperament (FET).

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Implicit behaviourism of neuroscience and psychology can't handle the complexity of neurochemical biomarkers

The organising principles of biobehavioral taxonomies (explaining 'why so', 'why these classes') should be based on biologically plausible theories and experimental evidence [19••]. This brief opinion paper suggests continuing ongoing efforts to examine existing and potential theoretical paradigms and formalisms, including principles of neuroscience. Neuroscience, being a relatively young science, still explores principles of biomarkers underlying consistent behaviour, and this, in turn, affects its taxonomic advice to biobehavioural sciences.

Therefore, in addition to experimental research, analytic discussions should be expanded in the psychology, psychiatry and neuroscience of biobehavioural individual differences. As part of these discussions of principle paradigms, one approach that should be probably abandoned is the 'stimulus → response' (S → R) paradigm of behaviourism ([1,2,63•, p. 175]). Behaviourism was condemned in various fields of psychology; however, it is very much alive in both psychology and neuroscience. For example, in neuroimaging, the discussions refer to brain connectivity and brain structures as they were a hardware that first learns the Ss and Rs (establishing the 'wiring') and then simply delivers the Rs, by analogy with radio circuits that process and transmit signals in communication devices. There are common discussions on how specific brain areas 'light up', or receptors get activated in response to experimental conditions. However, the accumulation of thousands of such associations doesn't seem to help in sorting through biomarkers of symptoms or traits. These associations appear to overlap for many brain areas and in many behavioural aspects; the associations also showed low consistency. More importantly, the implicit model 'event → brain structure activation' was unable to explain numerous phenomena, for example:

1) 'The degrees of freedom problem' outlined back in the 1930s by Bernstein in relation to construction of physical actions [63•, p. 105,69,70. P.354–355] and since then it was recognized in neuroscience as a universal challenge of behavioural regulation [3••,4••,5••]. This problem relates to the fact that nervous systems ignore 99.9% available stimuli (Ss) [68•] and suppress 99.9% of possible ways to 'react' (Rs) to make behaviour smooth and adequate. The main challenge for a nervous system is not to hardwire-specific Rs to specific Ss, but rather sort out through the myriads of degrees of freedom among Ss to determine which to attend to, and to determine which SS to

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respond out of the myriad of possible Rs. This means that in most cases, behaviour doesn't follow stimuli that individuals are exposed to (and, therefore, doesn't follow the S → R model).

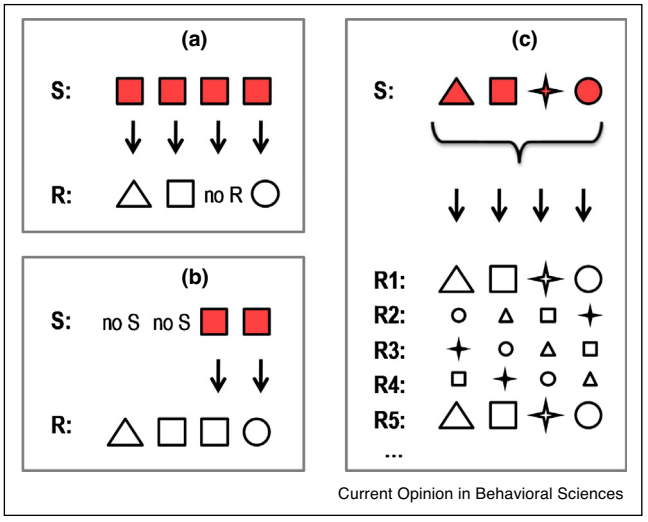
2) The diversity of Rs in response to the same Ss in individuals with a similar lack of experience (even in newborns) (Figure 1a) was noticed by Pavlov himself (i.e. from the origin of the conditioning paradigm). The individual differences in response to the same stimulation were, in fact, the primary reason why he shifted to studying biomarkers of temperaments in the second half of his career [64].
3) Even when people have learned a script for required actions (Rs), in many cases (commonly known in OCD or failed performances during exams or competitions), they launch different, often less adequate and less adaptive actions without any environmental factors that might explain this variation. In such cases, previously learned Rs, therefore, are not activated as expected but, as it is commonly known, new, exploratory actions are produced instead (Figure 1a, b) [63•].
4) Many actions are initiated without an obvious S (Figure 1b), for example, exploratory and creative actions (when a goal for future actions doesn't exist and so Ss are not identified).
5) Out of all situations we face and people we meet, most of them we face and meet only once. Without a previously established S → R association (or brain networks for that), we still handle these events fine, and it is doubtful that our nervous systems keep specific networks-memory for each of them for future use [68•]. After all, why do people facing the same situations/people again act differently?

As another example, neuroscience courses for university students give an impression of neurotransmitter receptors as as if they were switches that receive and transmit the signal and otherwise remain 'at the ready', with synaptic vesicles supposedly storing neurotransmitters (NT) until their release is needed. Graduates of such teaching investigate the action of agonists or antagonists for specific receptors assuming that receptor's responsiveness is the function of incoming Ss and properties of receptors; it is implied, therefore, that the action of the receptor is isolated from whatever the rest of the nervous system is doing.

In reality, there is no 'obedience to Ss' in neurotransmission [68•]. There are background neurochemical processes barely observed at the macro-level of brain anatomy, however, serving as the 'grey cardinals' of behavioural regulation:

First, most neurotransmitters and neuropeptides (NP) are not stored in synapses, ready for release, but instead are synthesized and immediately decomposed after use, with different mechanisms related to these cycles for each NT.

Figure 1



Filled (S) geometric shapes represent kinds of stimuli, and shallow shapes – kinds of actions. Implicit behaviourism in neuroscience cannot explain **(a)** individual differences in brain and behavioural responses (R), or absence of responses to previously learned stimuli (S); **(b)** many actions in behaviour or activation of brain areas and neurotransmitter release (R) are generated in the absence of supposedly relevant stimuli (S) or are inadequate for situations. **(c)** The illustration of how individual differences in capacities (depicted in a size of the shapes) create biases in behavioural orientation to specific reinforcers. Larger shapes symbolise higher probability of response, smaller — lower probability of response.

Second, NT release is also not a simple 'knock → gates open' process. It proceeds in several stages, and each stage involves a cascade of contingent transformations regulated by mediators such as GABA, Glutamate, G-protein coupled receptors, transcription and neurotrophic factors, enzymes, metabolites, ATP, calcium and other chemical systems, as well as the regulatory impact of NTs and NPs on each other [6••]. Similar complexity and contingent constructions were described in the action of opioid receptors (OR) [7••,8]. Therefore (and third), the success of each of these multiple stages is far from being guaranteed and depends not only on the availability of mediators but also on the physiological state of the body, of the supporting microglia cells, of the brain cells that manufacture the needed components, and of environmental factors.

Fourth, the idea that neurotransmitters serve as chemical 'antenna and switch' systems does not explain why the most common type of transmission is not the classic fast ion-ligand synapse but rather the G-protein-coupling mechanism (GPC). The GPC has a variable speed of response (between immediate effect and a few days) as it requires multiple protein mediators [9•]. This is not something that would be expected if the receptors should

mechanically pass a signal as fast as possible. Fifth, the mechanical view of transmission can't explain why humans have a diversity of NTs and NT receptors, plus hormones and neuropeptides as co-transmitters, and all of these NTs and their different receptors have a differential distribution and functionality in behavioural regulation. Sixth, there is increasing evidence that many NT systems use extra-cellular, volume (i.e. non-synaptic) transmission unrelated to S processing [10•,11•]. Both synaptic and nonsynaptic communication between interneurons were found concurrently happening in the neocortex, challenging the conventional model of synapse-only transmission and the S → R paradigm [12••]. In other words, most 'talk' between the members of neurochemical ensembles happen not in the form of neurons firing in response to current Ss but outside of those structures (i.e. outside of neurons and not bounded to specific brain areas) that neuroscientists commonly focus on. Finally, neurons were shown to coexpress transmitters with opposite functions, as in the case of glutamate and GABA [13••,14•] — disproving the view of neurochemical processes as simple chemical signal transmission devices. Moreover, receptors known to be primary for specific NTs showed occasional affinity to the 'wrong' neurotransmitters [15••,16•].

What can possibly go wrong in this paradoxically complex mechanism of a seemingly 'simple act of signaling' between two neurons? Everything! For example, there might be a deficit or excess of enzymes and transcription factors composing and decomposing NTs, variations in the presence of co-releasing NTs and NPs in the same cell, upregulation or downregulation of receptors.

The implicit S → R script, therefore, is commonly used in neuroscience in setups of experiments and interpretation of results, however this theoretical paradigm doesn't match the uncovered principles that drive neurophysiology of behaviour. Also, while discussing 'what's next' in biomarkers of consistent behavioural patterns (CBPs), it is useful to discuss why (and how) some brain areas [25,26•,27•,28,38,47•,52•,65] or NT-NP receptors [6••,7••,8•,20••,38•,47•,54••] manage to stay silent and nonresponsive during activation of their neighbours — there should be additional mechanisms for stopping the spread of the signal? After all, a 'silence is golden' principle can be very informative in analysis of functional differentiation within the systems regulating CBPs.

Goal-directedness of behaviour is overrated

Goal-directedness paradigm ('activity theory') views behaviour as pro-active [3••]. It is well-documented indeed that the goal of the action organises neural and psychosomatic processes, so the brain and the body select degrees of freedom using the goal's parameters. This is true for both conscious and automatic construction of actions. However:

1) there are multiple elements in behaviour that are not goal-directed and, in fact, are not approved by an individual. These elements are so multiple that we can't ignore their existence. Examples include staying in useless chatting, waiting, resting, watching TV programs that we don't like and watching only because we are too tired to reach the remote and look for something else . . . In addiction research, it is common to hear from addicts that 'they hate this stuff but can't stop their actions'; many behavioural patterns associated with symptoms of psychiatric disorders — obsessive thinking, crying, having bursts of anger (after promising never to do it again) — are all not associated with goals.
2) Very often, people don't have a well-defined image of the final target of their behaviour but just 'expose themselves to the flow'. This often happens during vacations, attending parties and even at work, in creative projects.
3) People's motives are determined not only by what 'is out there' to use and motivate them but also by internal capacities and states, including tiredness, dysphoria, heartburn, sore feet, and so on — that is, conditions interfering with setting goals and programs of actions. We can, of course, expand the definition of goal-directedness to a broad goal of 'just being'. However, the list of factors that limits a person's degrees of freedoms in behaviour, that is, organize the behaviour into meaningful sequences with beneficial outcomes, should include not just internal instincts of 'just being', and not just environmental demands but also capacities of the person (seen in temperament), previous history, developed habits and individually specific choices of environmental reinforcers, briefly outlined in the concept of Specialized Extended Phenotypes (see below) [48•].

In search of useful formalisms: imbalances, cycles, embodiment, what else?

The multi-level nature of behavioural regulation and the complexity of biomarkers of this regulation requires further work on useful formalisms [19••]. Here are several thoughts on this topic.

To unify the concepts related to consistent individual differences in behaviour, whether temperament and personality traits of healthy people, symptoms of mental disorders or anything in-between on this continuum, we suggested earlier to use the abbreviation CBPs for *consistent behavioural patterns* [47•,48•].

One of the oldest formalisms related to neurochemical biomarkers of CBPs is the concept of (neuro)chemical *dysbalances*. The Internet is full of misleading claims equating this concept with the idea of the brain having 'either excessive or insufficient chemicals, called neurotransmitters'. The original concept of (neuro)

chemical dysbalance (offered by the fathers of formal medicine Hippocrates and Galen 2000–2500 years ago) is totally different from this definition. Their concept considered an ensemble ('*temperamentum*' = 'mixture', *lat*) of chemical systems, not a single system. Indeed, as mentioned above, there are a number of NTs and hormones regulating human behaviour that also regulate each other's release, composition, storage, and decomposition. However, this is not a 'soup of everything with everything' since the coupling of NTs in such co-release is highly specialized between brain structures and projections [20••,21]. A consistent underproduction or overproduction of some components leads to specific variations in neurochemical regulation. This supports those ancient doctors' idea that dysbalances within (neuro)chemical regulatory systems can lead to consistent biobehavioural differences, including psychopathology. Healthy functioning involves moderate 'swings', from out-of-balance deviations in these productions (as, for example, in the case of serotonin reuptake during transmission within serotonergic receptors). Extremes in such out-of-balance states are linked with a number of psychiatric disorders with serotonin's role in depression and opioid receptors in bipolar disorder or addiction as prominent examples.

Temperaments and symptoms of psychopathology are based on the same neurochemical cycles, and the idea of a continuum between them [18•,55•,57••,60•] was supported by neurochemical correlates in the cases of cases of neuroticism [22,23], low endurance [24], rigidity (as low plasticity) [25,26•], impulsivity [27•,28,29], emotional dispositions [30••,31••], (low) empathic processing [32••,33•], compromised probabilistic (thought) processing [34], sensation/risk seeking [31,35,36•], and (low) sustained attention [37,38]. Tables 1 and 2 illustrate how this continuum can be formalized. The problem is not that the original concept of chemical dysbalances is invalid: indeed, all neurochemical systems operate as sequences of out-of-balance states, briefly returning to optimal points and soon leaving them, rather than staying in an individually consistent steady-state. Even the physiological and neurochemical systems of healthy, stable people oscillate between intake and release of water, air, food, information, social support, sleep-wake states and so on. Everything in neurochemistry is somewhat dysbalanced, and substantial dysbalances lead to psychopathology. The concept of dysbalances, however, is too general, and so needs to be complemented by more detailed formalisms in line with progress in bio-behavioural sciences.

Another formalism that comes to mind, considering the contingent composition-decomposition processes in neurotransmission and even the selective reinforcement nature of the individual-environment interaction, is the concept of *cycles*. Indeed, the processes driving both neuronal biomarkers and consistent behavioural patterns can be presented as a chain of swings between inter-connected pendulums that trigger, amplify or suppress each other, forcing these cycles to continue. Establishment of 'synergetic' cycles during learning of physical actions at several levels of behavioural regulation was also described by Bernstein [69,70, pp.174, 357–359]. This concept, however, is also insufficient to present all aspects be behavioural construction as it doesn't include processes outside of established cycles. There are many processes that could be considered as 'tried and failed' compositions or processes that are too variable to call them 'cycles' [3••]. Many people's intentions and promises do not end in promised actions; many times special training and experience do not lead to employment where the learned skills are needed; many times we start sentences without finishing them, instead replacing them with more adequate sentences. The same overproduction of 'bits' that are not used for future compositions is common at the neurotransmitter level [6••,7••,8•,9•] and includes volume transmission [10•,11•,12••]. The concept of a cycle, therefore, should be complemented by formalisms describing these failed compositions (let's call them *run-away processes*), successful but transient and variable compositions (*start-ups*) and several degrees of variation in established cycles. Besides, multi-pendulum mechanical models cannot explain the emergence of unwanted, unprovoked, creative, exploratory, 'first and only' actions, all constituting a large part of behaviour.

One more type of formalisms that can be beneficial to develop for the analysis of biomarkers for CBP taxonomies relates to the concept of *embodiment*, the idea that not just the brain but also features of the body regulate psychological processes. Studies in cognitive and personality psychology had confirmed the role of embodiment, when sex and temperament traits appeared to influence semantic perception (i.e. meaning attribution) in a very specific and consistent manner [39••,40•,41•,42]. In these studies, for example, people with stronger physical and social endurance gave significantly positive estimations to neutral common concepts than people with weak endurance, and people with higher neuroticism gave more negative estimations, in comparison to low-neuroticism groups [39••]. Remarkably, the embodiment principle was highlighted back in ancient times and was also part of Hippocrates' theory of 'temperamentum', emphasizing the role of bodily fluids in behavioural regulation. Modern findings of hormonal regulation involving endocrine glands and the emerging discipline of 'gut psychiatry' describing the contribution of microbiota to the regulation of the HPA axis fully support this idea [43••,44,45,46••]. Gut psychiatry and endocrinology, therefore, are essential disciplines that should be consulted in discussions on biomarkers of CBPs.

Table 1

The names of temperament components are marked in bold shadowed font, and associated neurochemical systems according to the neurochemical model Functional Ensemble of Temperament are marked in bold. Temperament components (T-CBP) are compared to clinical consistent behavioural patterns (C-CBP) related to high and low expressions of each component, in comparison to the Norm (N). The line "Context" lists contextual demands where a given CBP is observed the most. Emotional amplifiers induce dispositional approval (marked by !!) or disapproval and a request for search of behavioural choices (marked by ??). Disp: dispositional. Abbreviations of neurochemical systems are the same as in Figure 2.

Behavioural aspect:	*Beh. orientation & expansion of d.f.*	*Speed of integration of actions*	*Cycle maintenance systems*
CBP type	*Wide context, probabilistic, implicit aspects: MA, ACh, GG as leads*		
T-CBP ≈ N	**Probabilistic processing, PRO** **Glu, NE, ACh**	Ease of change in actions: **Plasticity, PL** **DA+ACh, 5-HT, GG**	**Mental** (Intellectual) **Endurance, ERI** **ACh, 5HT**
C-CBP < N	Low intelligence and comprehension	Rigidity (rituals in OCD)	Inability to focus as part of the ADHD
C-CBP > N	(possible) Narcissistic PD Part of schizophrenia	Excessive start-ups without finishing them (e.g. in ADHD, mania)	Obsessions, as part of OCD
Context	Complex, novel	Changeable	Requires monitoring
	Social-verbal aspects, tuning actions to other people: OXY, Estr as leads		
T-CBP ≈ N	**Empathy, EMP** **OXT+ VSP**	**Social Tempo, TMS** **DA+Estr**	**Social Endurance, ERS** **5-HT+Estr, H**
C-CBP < N	Autistic disorders	Expressive language problems	Social withdrawal
C-CBP > N	Dependent PD	Mania	Histrionic PD
Context	Resonance to others	Fast communication	Long communication
	Physical aspects, determined by physical capacities: 5-HT, ORE, H and NPs as leads		
T-CBP ≈ N	**Sensation Seeking, SS** **Tstr, NE/-Adr, -Cort**	**Physical (Motor) Tempo, TMM** **DA+GABA, A, ACh, NP**	**Physical (Motor) Endurance, ERM** **5-HT+ORE, H, NP**
C-CBP < N	Generalised Anxiety	Motor retardation and slowdown, Parkinson D.	Fatigue, sleep problems
C-CBP > N	Antisociality, to bust low HPA arousal	Physical agitation	Athletic ability for endurance
Context	Exceptional tasks	Fast physical routines	Long physical routines
	Emotional amplifiers: OR, HPA and GC as leads		
T-CBP ≈ N	**Neuroticism, NEU** **KOR, GC>MOR** **KOR→NE-HPA,**	Spontaneity, **Impulsivity, IMP** **Tstr, DOR→(DA, MOR)**	(Disp) **Satisfaction, SF** **MOR>KOR, GC** **MOR→(5-HT,DA)**
C-CBP < N	Indifference, detachment	Inability to be playful or spontaneous	Dysphoria, pessimism, low confidence
C-CBP > N	Low tolerance to novelty/uncertainty, perceptual alertness	Premature integration of actions, behavioural reactivity, impulsivity	Too relaxed dispositions, over-optimism
Context	Uncertainty	Emergency	Safety, support

Functional constructivism: possible applications to CBP taxonomies

More inclusive and fruitful formalisms compatible with goal-directedness and 'just being' behaviour, in our opinion, could be developed using the *Functional Constructivism* (FC) paradigm [3••,30••,47•,48•] and the concept of *Specialized Extended Phenotype* as a part of FC. As a contribution to the discussion of principles underlying behaviour, the brief message of this paper is: behaviour is not reactive; (often) not pro-active (goal-directed), but it is constructive [3••,47•,48•]. The FC approach suggests that:

1) All behaviour is not reactive but constructive: all actions are constructed anew as the integration of behavioural capacities, needs and alternatives that were selected and sequenced for their relevance across multiple levels of behavioural regulation (Figure 2). Even when consistent behaviour looks like cycles, habits and repetitions of identical actions, it is actually never repeated but instead uses similar compositions of previously established sets of behavioural elements. This generative, constructive nature of behavoiur and memory was noticed at many levels of behavioural

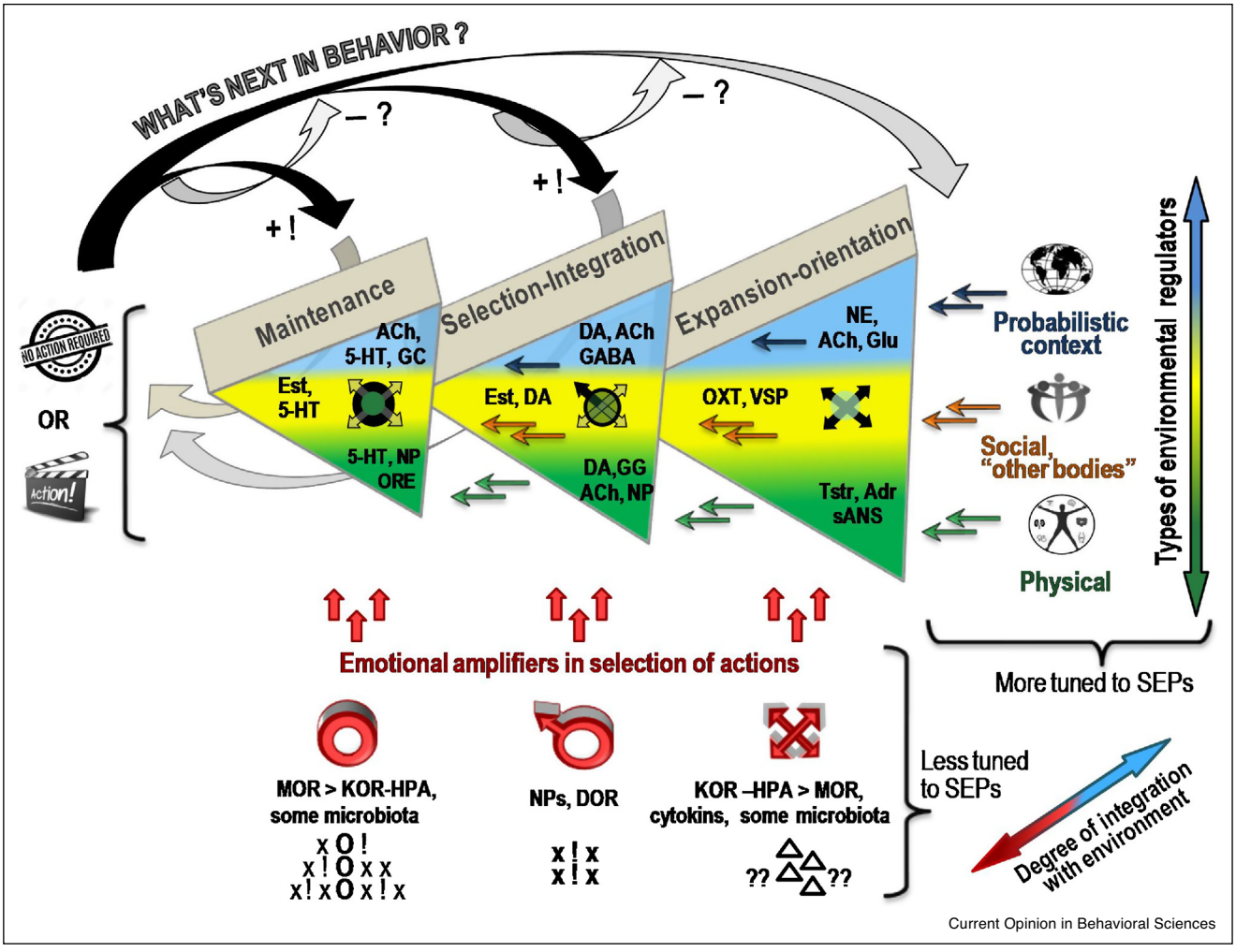
Table 2

Proposed correspondence between described neurochemical systems, temperament components of the FET model (see abbreviation of components in Table 1) and main diagnoses of psychopathology. References to the studies using FET-structure test STQ-77 on clinical samples could be found in [48•]. Note: ↑ — higher than optimal and ↓ (shadowed-(yellow in color print)cells) — lower than an optimal expression of the system and temperament traits. * — proposed but not confirmed in the study

ICD	ICD *FET:*	*NEU*	*IMP*	*SF*	*SS*	*TMM*	*ERM*	*PRO*	*PL*	*ERI*	*EMP*	*TMS*	*ERS*
6A7Z	Depression/ Dysth	↑	↑	↓		↓	↓		↓	↓		↓	↓
6A60.2	Hypomanic Bipolar 1		↑	↑	↑	↑						↑	
6B23.Z	Hypochondria	↑					↓	↓	↓				
6B2Z	OCD	↑	↓		↓			↓		↑			
6B00	GAD	↑	↑					↓		↓		↓	↓
6B01	Panic Disorder	↑		↓			↓			↑			↓
6B03	Specific Phobia				↓			↓					
6B04	Social Phobia	↑		↓					↓		↑	↓	↓
6B02	Agoraphobia	↑		↓	↓			↓	↓			↓	
6B40	PTSD	↑	↑					↓	↓				↓
6B43	Adjustment Dis	↑	↑	↓		↓	*	↓	↓				
6B8Z	Eating Disorders	↑		↓				↓		↑	↓		
6A20.Z	Schizop, Paranoid	↑	↑	↓				↓			↓	↓	↓
6A20.Z	Schiz, Cataton.				↓	↓			↓	↓	↓	↓	↓
6A20.Z	Schiz., Disorgan-d		↑					↓	↓	↓	↓		
6A24.Z	Delusional Disord	↑						↓	↓	↑			
6A02.Z	Autistic Disorder		↑		↑	↑			↓		↓	↓	↓
6D10.Z	Paranoid Pers.Dis.	↑		↓				↓	↓	↑			
6D10.Z	Schizoid PD							↑	↓	↑	↓		↓
6D10.Z	Schizotypal PD	↑		↓				↓			↓		
6D10.Z	Narcissistic PD	↓		↑							↓		
6D10.Z	Histrionic PD	↑		↑							↓		↑
6D11.5	Borderline PD		↑	↓	↑			↓		↓			
F60.2	Antisocial PD		↑	↑	↑	↑					↓	↑	
6D10.Z	Conduct Disorder	↓	↑	↑	↑	↑		↓	↑	↓	↓		
6D10.Z	Obsess-comp PD		↓				↑		↓	↑			
6D10.Z	Dependent PD	↑		↓	↓		↓	↓	↑		↑		↓
6D10.Z	Avoidant PD	↑		↓	↓			↓				↓	↓

regulation for at least a century within different bio-behavioural sciences, first in kinesiology [4,5,63•, 69,70] and then in neuroscience [7••,49,50•,52•,65, 66,68•], cognitive [53•,71••,72••,73••] and social [74] psychology psychology of emotions [3••,30••,31••,50•] and other behavioural sciences (see Refs. [3••,47• for reviews]. For example, as noted above, neurotransmission at the cellular level proceeds through the multi-stage selection, construction and decomposition of participating chemicals [6••,7••,8•]. At the level of neural networks, it has been shown that brain connectivity is highly plastic and that neuronal ensembles of the brain re-organize themselves, and/or reorganize their electric activity following a change of situational context and task [49,50•,68•,72••,73••]. A generative dynamic is well-known in gene transcription. Phenomena of cognition (perception, memorization, recall, comprehension) also appeared to follow similar selection-construction principles [71••,72••,73••], with Bartlett deserving a credit for highlighting the (re-)constructive nature of memory retrieval [53•] in the 1930s. Finally, at the level of behaviour, Bernstein's work in the 1930s described multiple examples of the principle 'repetition without repetition' in generation of actions [63•, p. 204, 436]. This principle suggests that actions, no matter how much they were pre-learned, are composed (often at multiple level of behavioural regulation) afresh based on an individual's previous actions, current capacities, intentions and situational context [63•, p.243, 436,69,70, p. 358–365; 538–540].

Figure 2



Neurochemical model Functional Ensemble of Temperament is presented here describing a progression (arrows) in the selection of behavioural alternatives in three approximate stages of generation of behaviour. When the first (maintenance) cycle cannot be accepted as adequate to a situation, a re-integration of existing behavioural alternatives (2nd stage) or a search for new/additional alternatives (orientation, 3rd stage) develops. Novel/complex situations activate more behavioural orientation systems than well-learned and simple actions, however every action has all three types of systems involved to some degree. 'More tuned to SEP' in selection of actions means a higher degree of influence of this selection by environmental functional 'bubbles' that an individual is involved in; 'less tuned to SEP' means that selection of actions is more influenced by the body's state. There is an interaction between neurochemical teams within and across these stages (triangular shapes). Three emotional amplifiers (three bottom shapes) influence this selection (vertical arrows) coinciding with the functionality of each stage. The '+!' and '–?' signs at the top and the bottom sections of the Figure show the trends to either accept or not accept (correspondingly) behavioural alternatives, amplified by the action of MORs for acceptance and KOR for continuation of a search of alternatives (influencing each stage). Note: MA: monoamines (NE, DA, 5-HT); ACh: acetylcholine; NE: noradrenaline; 5-HT: serotonin; DA: dopamine; OXY: oxytocin, VSP: vasopressin, Tstr: testosterone; Adr: adrenalin (and its deficient cycles); GC — glucocorticoids (including cortisol dysregulation); ORE: orexins; NP: neuropeptides; Glu — glutamate; GG — Gamma-Aminobutyric Acid and Glu; (M/D/K)OR: (mu/delta/kappa) opioid receptor systems; sANS — sympathetic autonomic nervous system; SEP: Specialized Extended Phenotype as a part of environmental infrastructure compatible with individual's capacities.

2) The FC generative principles explain the composition of novel actions in the absence of S (Figure 1b), the composition of wrong actions after learning the correct R (Figure 1a, b) and resolve the 'degrees of freedom problem'. Still, if there are no 'stored units' anywhere in the nervous systems that exist on 'stand-by' mode and operate upon demand from stimuli, then how can we explain consistent behaviour, learning and memory? It has been shown that novel actions are composed with significant involvement of the frontal cortex, which communicates with the ventral striatum to develop a program (sequence and choice) of actions.

Then, with the increase in certainty of the program of actions and learning (with habit formation), control over the integration of action is passed from the ventral to dorsal striatum [51••,52•]. Conversely, with an increase in complexity of the task, control over integration is passed to the ventral-striatal-cortical and cerebellar networks [52•]. What are observed as habits, therefore, are behavioural compositions regulated by the dorsal striatum and cerebellum. Consistency in behaviour is observed due to the similarity of constructed actions in various settings. A similar transition between levels of behavioural regulation was experimentally described in work of Bernstein [63•,69,70] (he described five levels). The established neurochemical loops and networks supporting habits are too diverse, too numerous and too immature to be 'pulled into action' without additional trimming and selection for fitness to the context of situations [63•,68•,69,70]. That is where the nervous system shows its main functionality: in the selection of behavioural elements and then sequencing (integrating) them into actions.

3) The application of FC to CBP taxonomies was implemented in the neurochemical model Functional Ensemble of Temperament (FET) that summarized the most conservative findings regarding the functionality of neurotransmitters, hormones and opioid receptor systems [17•,30••,47•,48•,54••] (Table 1 (grey lines), Figure 2). This model follows the three main aspects of action construction: selection/integration of a program of action, expansion of degrees of freedom (orientation) and energetic maintenance (including decomposition of unneeded degrees of freedom) (three columns of Table 1). These three aspects of behavioural regulation were noted from the mid-20th century in multiple biobehavioural sciences (kinesiology [63•], clinical neuroscience and functional psychophysiology) (see for Refs. [3••,17•], reviews and further references), but then, as noted above, the same types of processes occur at the level of composition, selection and decomposition of neurotransmitters.

The two middle rows of the FET (related to physical and verbal-social aspects of behaviour) describe more learned and more determined aspects, whereas the top row — probabilistic aspects, occurring in complex and/or novel situations. There, the development of formalisms for these universal aspects of constructive systems might be fruitful for future analysis, classification and modeling of behaviour [3••,47•,48•]. The FET is not the first model that suggests classifying CBPs using functional stages of action construction: a similar idea was proposed by Rusalov using slightly different components in the 1980–90s [56•]. Moreover, the FET follows the *activity-specific approach* to taxonomies of temperament that differentiate between biomarkers regulating physical, verbal-social, and mental aspects of behaviour [17•,54••,57••] (three top rows of Table 1; three corners of the triangular shapes of Figure 2). The validity of this approach is supported electrophysiologically [56•], neuroanatomically (by the functional specificity of brain areas regulating physical, verbal and probabilistic aspects of behaviour) [65,66], neurochemically (by the specificity of hypothalamic hormones differentially regulating social and physical aspects of behaviour) [31,58•,59•,67] and clinically (by differentiating between major psychiatric diagnoses) [55•,57••, 60•,61••].

4) FC also embraces the concept of *embodiment*: it is ultimately the body that performs the behaviour, and so body-related individual differences must affect consistent behavioural differences. For example, the roles of endorphins binding to mu-opioid receptors in moods and stress suppression is well known [7••,8•,30••,31••], but they are produced mainly by the body, in tight cooperation with immune and gut micribiota systems. Glial cells, that control the production of the most common NT — glutamate, are also tuned to the state of the body. In order to produce glutamate, they have access to blood supply of precursor amino acids produced in liver and body's metabolites [66]. Moreover, the core brain structure serving as a bridge between bodily neurochemical systems (endocrine glands, gut microbiota) and brain systems is the hypothalamus (HT). The role of hypothalamic neuropeptides and hormones in behavioural regulation was extensively described in the endocrinology literature, but Panksepp and colleagues should be praised for highlighting this role in the psychology of individual differences [67]. HT hormonal systems represent another good example for the embodiment principle as their status appears to be an important factor in temperament traits related to behavioural orientation, such as empathy [31,32••,33•] and sensation seeking [31,35,36•].

Functional partitioning of the HT and pituitary support the activity-specific approach to CBPs described two paragraphs above: hormones regulating social-affiliative aspects (oxytocin and vasopressin), and physical aspects of behaviour (Growth Hormone and somatostatin) are released from different parts of the pituitary and regulated differentially by the HT [58•,59•]. Therefore, a separation between biomarkers related to physical, social aspects of behaviour and probabilistic processing might be beneficial for CBP taxonomies (i.e. for classifications of temperament and psychopathology components).

5) The FET uses a '*multimarker*' approach, suggesting that there is no one-to-one correspondence between a specific CBP and any neurochemical system. Instead, every psychiatric symptom or temperamental (bio-behavioural) trait is associated with a team of

neurochemical systems (Table 1) [17•,30••,31••, 47•,48•,54].

6) The FET follows the idea of a health-clinical continuum [18•,55•,57••,61••] unifying healthy neurochemical regulation (seen in temperament traits) and various degrees of dysregulation, including the clinical spectrum seen in psychopathology. Since the FET uses the universal architecture of the way an action is constructed, its structure is applicable to any behaviour, no matter how dysfunctional this behaviour is. The Tables 1 and 2 illustrate how classic symptoms of psychiatric disorders can be mapped into the 12-component-FET framework. These components represent 12 biomarker systems verified both neurochemically and neuroanatomically (see Refs. [17•,30••,31••, 47•,48•,54] for reviews). The volume doesn't permit to go into details but such verified associations are listed in the grey bold font in Table 1. Examples include the role of ACh-NE systems in sustained attention, or the role of cortical-striatal DA systems in plasticity and speed of integration of actions (including speech). Each action is regulated by all 12 components to some extent but some components take the lead (see Table 2 for examples).

The concept of Specialized Extended Phenotypes (SEP) might be useful for biobehavioural taxonomies

The environment is a major partner in behavioural construction not only because it stimulates or suppresses actions but because it also provides an infrastructure assisting the selection, integration and support of actions. Animals and humans use this infrastructure for the extended storage of resources, extended memory, external mechanisms of information coding and retrieval (marking the territory and bonding in animals or using culture in humans), for decision making, sequencing actions (by imitating parents or peers), development of preferences, and so on. They do not merely utilize environmental resources but, in return, actively build and select elements of this infrastructure that later determine and organize their choice of actions. The evolution of nervous systems in tune with such 'external infrastructure' was summarized by Dawkins in the concept of *extended phenotypes* [62]. This concept was further developed into the ideas of Specialized Extended Phenotypes (SEP) [47•,48•] and diagonal evolution [3••]. SEP theory acknowledges the fact that people use environmental resources and regulators differently, depending on their capacities and needs (Figure 1c). For example, people with high learning and analytic abilities look for sources of knowledge and ways to share their ideas; athletic people look for physical challenges; people with high sociability — for social media activities; hypochondriacs — for health-related services and information, and so on. Despite equal access to various activities in civil societies, people use only a small portion of this access, mostly compatible with their bio-behavioural abilities, living in individually shaped functional cycles, socio-ecological 'bubbles' formed by their bio-behavioural capacities.

These personal SEP-bubbles include individually preferred settings, objects, partners, friends, social and professional networks as their regulators, compatible with their capacities and needs. This affects the selectivity of their response to the same set of stimuli (Figure 1c). In turn, the participation of people in specialized services and networks contributes to the evolution and reinforcement of these functional bubbles, with specialized infrastructures supporting the specific needs and abilities of each type of person. There are, therefore, two-way mutual selection and reinforcement influences between the types of neurobiological capacities and the environmental infrastructure that can generate segregated functional cycles, 'functional bubbles', defining the routines that an individual is involved in the most. In this sense, behavioural regulation only partially depends on either the composition of brain neurophysiology or socio-cultural pressures; importantly it also depends on compatibility between those two groups of factors.

Since all behaviour is context-dependent, our work on biobehavioural taxonomies should consider biases in behavioural choices affected by individual SEP cycles in people's routines. The 12-component FET network can be applied to the classification of contexts, assessing situations in terms of demands for energetic capacities, the flexibility of behaviour, information processing, each analyzed separately for physical, social and mental aspects of behaviour; also situational uncertainty and urgency (Table 1). Personal and professional history is the source of information about the individual's SEP, so it should be structured and formally assessed. The SEP concept also can accommodate a combination of goal-directed and 'just being' behaviour as SEP defines selectivity in people's choice of regulators for actions.

For the discussion of 'what's next', as specifically requested for this Theme Issue, it would probably beneficial to organize Advanced Study Institutes (similar to two-weeks NATO Scientific Committee meetings) to educate PhD non-neuroscientists about the nature of biomarkers underlying psychiatric symptoms and temperament traits, to facilitate development of biobehavioural taxonomies and multidisciplinary cooperation. Many universities don't have neuroscience training for psychologists, and it would be beneficial to offer such training. One of the topics in these programs should be the illustration of constructive, transient nature of neuronal neurophysiological systems. Because of the complexity and multi-level regulation of CBPs, multi-disciplinary cooperation is a 'must'. Multi-disciplinary summer

schools for mature scientists, specialists in their fields, as well as bi-disciplinary or multi-disciplinary meetings would be beneficial for the progress in biobehavioural taxonomies. Modern technology also offers a possibility of online platforms where scientists could not only deposit data but also outline alternative hypotheses and their justifications (let's call this idea 'project Socrates', to underline the analytic, debates-oriented purpose of this project). Moreover, considering the extreme complexity and transience of 'fluid' systems of neurobehavioural regulation (neurochemistry, gut biota, immune system), it might be useful to have a specialized Task Force or also an online platform analysing biomarkers specifically related to these systems (let's call it 'Hippocrates', honouring the author of the idea of biochemical origin of temperament).

Conclusions

In conclusion, this brief opinion paper suggests the FC alternative to implicit behaviourism in psychology and neurosciences. The analysis of how the transient nature of neurochemical biomarkers can produce stable, consistent behavioural patterns should be given no less priority than structure-focused neuroimaging. After all, the brain structures that are seen in neuroimaging as 'lighting up', are made of nothing else but these transient 'soups' of constantly changing neurochemicals, appearing and disappearing receptors, frequent failures to transmit a signal or transmissions depending on mass action of other synapses and extra-cellular and intra-cellular mediators. The Functional Constructivism approach presents behavioural products as selected out of multiple alternatives based on internal capacities and external regulators. Moreover, these products are consistently specialized according to an individual's preferences for specific elements of their environment rather than being exclusively dictated by universal environmental demands. Proper diagnosis of CBPs, therefore, should include a person's functional SEP cycle. The paper proposes a 12-component classification of psychiatric symptoms and classification of contexts based on the FET framework.

Conflict of interest statement

Nothing declared.

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