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# Unified neural structured model: A new diagnostic tool in primary care psychiatry

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ABSTRACT

Overlap of multiple mental disorders in each psychiatric patient has been emphasized and the style of assessment and intervention in each patient has been gradually changed. A new practical structured model that can comprehensively explain and assess the major mental disorders integratedly has been desired.

In this report, the relationships between each of the major mental disorders and each neuropsychiatric component like personality, reward system, or reinforcement learning have been comprehensively reviewed to construct a new integrated structured model for assessing the overlapped mental conditions in primary care psychiatry. This new structured model contains the following three loops: "input-output-feedback loop" (external/environmental loop), "reward-learning loop" (learning loop), and "mood-reward sensitivity loop" (mood loop), which are connected by the functions of prefrontal cortex and basal ganglia. With this new concept, overlapped mental conditions in each psychiatric patient could be theoretically much simply and logically explained.

In conclusion, with the proposed psychiatric structured model, we can simply explain and understand the overlapped mental disorders in each patient. Inventing and developing such basic psychiatric structured model would offer us new diagnostic and therapeutic tools to realize personalized medicine, especially in the field of primary care psychiatry.

## Background

The mental illnesses are presently diagnosed with clinical manifestations and include disorders like schizophrenia spectrum disorder, mood disorders (bipolar/depressive disorder), personality disorders, eating disorder, panic disorder, obsessive compulsive disorder (OCD), substance use disorders, and neurodevelopmental disorders [1]. These mental disorders were once regarded as globally different, independent disease entities in the previous versions of DSM [2]. In the latest version (DSM-5), overlap of these mental conditions has come to be paid more attentions and dimensional measures for psychiatric symptoms have been applied, but the applicability of such operational diagnostic criteria to the assessment of overlapped mental disorders and to the therapeutic approach in each patient is not clear. Under this latest concept, mental disorders that were once regarded as different disease entities are now regarded to be possibly overlapped with continuous phenotypes; psychiatric symptoms in each patient has come to be multi-dimensionally assessed with the percentages of coexisting multiple spectrums [3]. To understand the appropriate therapeutic approach in each psychiatric patient and promote personalized medicine in clinical psychiatry, we need to scientifically develop a basic neuropsychiatric structured model that can comprehensively explain the overlapped mental conditions in each patient. In this report, for the first time, a new evidence-based neuropsychological structured model to comprehensively explain the major mental disorders will be proposed.

## Main text

### *Framework of the structured model*

#### *External input, output, and personality*

A personality can be described as a property of the way of perception and procession; it responds to the extrinsic factors (external inputs) like given social tasks, stressors, or required social involvements [4,5].

*Abbreviations:* ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; D1/D2, dopamine receptors; DSM, diagnostic and statistical manual of mental disorders; IQ, intelligence quotient; LD, learning disorders; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder; $R(t)$, transmitted strength of reward signal newly released at the time of "$t$"; $R_{accum}(t)$, accumulated amount of transmitted reward signal at the time of "$T$"

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Properties of personality can be defined from various viewpoints containing psychology and psychiatry; one of the promising categorizations is the following "big five personality traits": openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism [6–8]. These functions of personality are supported and enhanced by preserved memories (mainly referring to the declarative memory in the classification by Squire & Zola-Morgan) and achieved intelligence. These neuropsychological components cooperatively and intermittently process the external inputs to perform satisfactory outputs throughout life [9–11]. The resulting output would eventually result in the next input from the environment as positive- or negative-feedbacks and would continuously bring variable secretion of reward stimulants.

Generally, external inputs are multiple, multifactorial, and multimodal; thus, it must be recognized as a multi-dimensional vector quantity. For example, given tasks and stressors are to be recognized at least with the following components: types, amounts, difficulty, allowed time, priority, and anticipated amounts of the reward [12,13]. After recognizing the properties of the given tasks, the personality collates the inputs with the preserved memories of previous experiences, which would be paired with the information of achieved rewards, and decides the response to the given inputs [10,14,15]. The information of this output would be still multidimensional, though the number and types of the output could be changed from those of the input.

These transformational algorithm would be strongly affected by the developed personality traits, which is comprised of very complicated multiple components. For example, the social behavior is based on not only selfish manner but also altruistic manner [16–18]. Altruistic behaviors within a group of genetically close relations can be explained by the function of selfish gene and kin selection. On the other hand, to practice reciprocal altruism in the society, accumulation of successful experiences and observational learnings, facilitated by domestic environment, would be important to achieve matured personality and viewpoint of social reciprocity [19,20].

When building a structured model that process external inputs to achieve satisfactory outputs, the functions of the human brain would be described with the congenital or acquired properties of the following neuropsychiatric steps: perception, personality, intelligence, and memory. At this point, we can assume a loop circuit comprised of external inputs (*i.e.* task, feedback), perception, processing personality and intelligence, and derived outputs (*i.e.* action, behavior), which is strongly supported by preserved memories. Anatomically, the prefrontal cortex (PFC) is known to play important roles to realize these advanced personality traits [21]. Memory would be mainly localized in the Papez circuit, but many other structures including amygdala or cerebellum are also associated in modulating the memory.

We can add an extra step of "perceiving filter" at the first step of perception, which would screen and weight the external inputs at the very first point [22,23]. Though this step could be included in the personality, several mental disorders certainly show impairments between the steps of sensory input and perception [24–26]. Thus, at this report, we assume an independent step of perceiving filter different from the steps of perception and personality.

At this point, we can depict a neuropsychological loop structure comprised of inputs, filter, perception, personality, and outputs, as shown in Fig. 1. The main external components of this loop structure are the social and family environments. We can call this continuous loop as "input-output-feedback loop" or "external/environmental loop". Based on this architecture, the essence of intelligence could be described as the long-term accuracy of reward anticipation and proficient utilization of preserved memory by the prefrontal cortex.

*Reward system with reinforcement learning*

In the nervous system, reward system is known to play a key role in realizing the reinforcement learning and in establishing the environment-dependent algorithm to decide the appropriate behavior [27,28]. Secretion of dopamine plays a key role in these functions [28,29]. The reward system is known to be anatomically locating around basal ganglia, projecting synapses toward PFC and amygdala [30]. Both of the secretion of dopamine and the distribution of its receptors in the reward system would play essential roles in reward system [31]. The dimension of the derived reward signal would be much lower than that of the original external inputs, though whether the reward signal can be regarded a single scalar quantity or not is not known.

Projectile nerves from ventral tegmental area to nucleus accumbens is known to be associated with an anticipation of expected rewards [32,33]. The reward anticipation is believed to be enabled by the preserved paired memories of selected output and acquired reward for each external input [34–36]. Both of personality and accumulated memories are necessary in anticipating expected rewards. The reward signals eventually affect the processing algorithm in PFC, which is known as "reinforcement learning" [28,37,38].

By this point, we can depict a structured loop comprised of personality and reward system, as shown in Fig. 2, which can be called as "reward-learning loop", or simply "learning loop". In this figure, $R(t)$ stands for the strength of transmitted reward signal released at the time of "$t$".

$$R(t){:}\ = Transmitted\ reward\ signal\ at\ the\ time\ of\ \text{"“"}t\text{"”"}$$

To continually maximize the acquired amount of reward signal with reinforcement learning, personality would continuously develop and adapt itself to the environments based on the rate of change in $R(t)$.

$$Reinforcement\ learning \propto \frac{dR(t)}{dt}$$

As described above, $R(t)$ would be regulated by both of the amount of secreted reward stimulants (*e.g.* dopamine) and expressions of the receptors [37].

*Mood and reward sensitivity*

The accumulated amount of reward signal at a specific time would also affect the efficiency of learning and would affect the mood [39,40]. Here, the accumulated amount of transmitted reward signal at the time of "$T$" ($R_{accum}(T)$) can be described as the convolution integral of the function of reward signal ($R(t)$) and its attenuation function ($A(t)$).

$$R_{accum}(T) = \int_0^T R(t)\cdot A(T-t)$$

As previously known, a positive mood condition increases the efficiency of learning, creating a positive-feedback circuit comprised of reward system and mood [39,41]. This concept matches the fact that dopaminergic signal creates a positive feedback loop [42]. On the other hand, as described in the next section, impaired mood conditions is known to result in abnormally elevated corticosteroid level. This corticosteroid, also known as stress hormone, suppresses the reward sensitivity as a negative-feedback [43].

With these positive- and negative-feedback loops, reward system and mood condition are closely related each other. Different from the above-mentioned "reward-learning loop", this loop functions with relatively longer time period, because it requires changes in the expression of dopamine receptors in the related anatomical sites of the reward system.

Based on these concepts, we can depict a structured loop model connecting reward signals, mood conditions, and reward sensitivities, as shown in Fig. 3. In this report, we call this loop as "mood - reward sensitivity loop", or simply "mood loop".

*Overview of the invented structured model*

With the above-described three loops shown in Figs. 1–3, we can depict the overview of the comprehensive neuropsychiatric structured model as shown in Fig. 4. Upper half of this architecture mainly