

Neuroeconomics and General Neural Biomarkers

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Abstract. The study reviews neuroeconomic studies of Frontal integration with a view to identify components of relevance to decision-making.

Results: Four different partitions of the Frontal Cortex are identified as relevant to integration: Ventromedial Prefrontal Cortex integrates emotional drives from the Mesolimbic dopamine system by inhibition of Orbitofrontal Cortex and activation of cognitive analysis by Dorsolateral Prefrontal Cortex (dlPFC). Prospective decisions are maintained as pending goals in the Frontopolar Cortex. dlPFC is served by semantic memories recollected from Temporal Cortex and a visuospatial sketchpad in the Parietal Cortex.

Conclusion: Frontal integration balances a reinforcing mesolimbic value system with Neocortical value prediction. General neural biomarkers are identified: 1) Emotional stress arising from the conflict of Limbic and Frontal systems is indicated by the basal heart rate variability and 2) Cognitive stress arising from overloaded goal-direction by dlPFC may be indicated by the basal galvanic skin conductance balance of hands.

Keywords: Neuroeconomics, neurocybernetics, biomarkers, neuroimaging, brain model, stress, biofeedback, galvanic skin conductance.

1 Introduction

Classical neurology divides the central nervous system (CNS) in the Cortical sensory-motor integration system and the sub-cortical autonomic nervous system. McLean [1] and Luria [2] already advanced integrated brain models in the 1970es. The quantum leap in the last decade on resolution of neuroimages by modern magnetic resonance scanners enables a neurological study of ordinary decision-making processes by fMRI e.g. related to economic choices. Such integrated behavioral science termed neuroeconomics is emerging as an interdisciplinary field between neuroscience, psychology and economics. A neuroeconomic review focusing neurocentres of common interest to economists and psychologists identifies Ventromedial Prefrontal Cortex (vmPFC) as relevant to decision-making (DM) under uncertainty, Dorsolateral Prefrontal Cortex (dlPFC) as relevant for intertemporal choices and Orbitofrontal Cortex (OFC) as relevant for social DM [3]. This definition of neuroeconomics guides the study.

On this background we have firstly searched for evidenced parameters of Frontal DM. Then we have proceeded to relate these parameters in a neuroeconomic model (NeM) as the core goal of the study. Finally, NeM is validated against some clinical challenges.

2 Method and Materials

Classical one-way causation is not appropriate for brain models as the brain are known to function by feedback loops (cybernetics). Neurocybernetics borrows the methodology of computer programming working within a framework of client-server-integrator relationships (Cybernetics of the 2nd order). Study materials are identified searching Medline and PsychInfo for: ‘Frontal lobe’ AND ‘Neuroeconomics’.

Table 1 Studies on Neuroeconomic Subdivision of the Frontal Cortex

Study	Function
<p>Ventromedial Prefrontal Cortex (vmPFC) <u>Ernst et al</u> [4] propose a review based Triadic model of motivated behavior to determine the balance between reward-driven and harm-avoidant behavior. Distributed neural circuits associated with this system are: 1) vmPFC and 2) Nucleus Accumbens (NAcc) and Amygdala (Am) in the Limbic System. <u>Camille et al</u> [5] conclude from a fMRI-study that damage in vmPFC more likely make choices that are inconsistent with value-maximization <u>Oya et al</u> [6] found by EEG a robust alpha-band component of event-related potentials in the vmPFC that reflected the mismatch between expected and realized outcomes in the task which correlated closely with the reward-related error obtained from a reinforcement learning model of the patients choice behavior.</p>	<p>vmPFC as Cognitive Integrator</p>
<p>Dorsolateral Prefrontal Cortex (dlPFC) <u>McClure et al</u> [7] concludes from a fMRI-study of intertemporal choices the involvement of separate neural value systems for immediate and delayed monetary rewards. Delayed rewards are dominated by dlPFC while immediate rewards are dominated by the Mesolimbic Dopamine System (MLDS) <u>Sanfey et al</u> [8] also concludes from a fMRI-study of the Ultimatum Game the involvement of both the dlPFC and MLDS in human monetary choices.</p>	<p>dlPFC as Prediction Centre activated by vmPFC</p>
<p>Orbitofrontal Cortex (OFC) <u>Beer et al</u> [9] concludes from a fMRI-study of betting game that activity in lateral Orbitofrontal Cortex is associated with evaluating the contextual relevance of emotional information for decision-making which is controlled by vmPFC (BA47). <u>Zald 2009</u> [10] concludes from fMRI-studies that several brain regions play a role in the valuation and comparison process of food selection. Among these OFC. This influence on positive and negative valuation is critical in designing diets and public health programs promoting healthy eating. <u>Camille 2004</u> [11] concludes from a gambling trial with affective rating and measurement of Galvanic Skin Conductance that facing the consequences of a decision trigger emotions like satisfaction, relief and regret by counterfactual thinking. This documents the integration of both vmPFC, dlPFC and OFC.</p>	<p>OFC as Preference Centre controlled by vmPFC</p>
<p>Frontopolar Cortex (FPC) <u>Koechlin&Hyafil</u> [12] has reviewed research in FPC. They conclude that the FPC is a pending long term memory for the ongoing synthesis of two neighbouring regions: OFC and dlPFC. Patients with lesions in FPC show normal perception, language and intelligence, but appear markedly impaired in decision-making in open-ended and ill-structured situations. <u>Daw et al</u> [13] concludes from a fMRI-study of a gambling task that the FPC is active during exploratory decisions as compared to exploitive decisions.</p>	<p>FPC as Pending Memory for long term goal</p>

3 Results

3.1 Ventromedial Prefrontal Cortex as Cognitive Integrator

Inferior Frontal Gyrus (vmPFC) inhibits arising emotions from MLDS by OFC [9] which enables cognitive analysis by dlPFC [7-8]. This constitutes vmPFC as cognitive integrator denoted \mathbf{c} in our model. Besides the three partitions identified [3] the literature review has added FPC as the highest and ethological most recent brain center. FPC maintains long term goals as a pending prospective memory of DM [12] denoted \mathbf{C} in our model. This core model of Frontal integration may intermediately be formulated in the following way:

$$\mathbf{C} = f[(dlPFC * \mathbf{c}) / (OFC / \mathbf{c})] = f[(dlPFC * \mathbf{c}^2 / OFC)] \quad (1)$$

The next objective of the study is to uncover the neurology of dlPFC and OFC in DM.

3.2 Meso-limbic Dopamine System as Client

The mesolimbic dopaminergic system (MLDS) is a neural network of dopamine cells rooted in the Basal Ganglia passing the Thalamic Nuclei through Frontal Cortex. MLDS is internally coordinated by Hypothalamic homeostasis and ruled by an autonomic pleasure-seeking disposition [14]. Reinforcement learning by MLDS is closely associated with experiences recognized by Hippocampus (Hip) [15-16]. The crucial importance of Hip to stabilization of MLDS is demonstrated by an fMRI-study of neural responses to pleasant versus unpleasant music [17]: Over time during the presentation of musical stimuli activations increased in all structures but Hip which decreased activity.

The Anterior Cingulate Cortex (ACC) is a primary centre of consciousness mirroring the actual emotional state (mood) in an emphatic way as we respond nearly as strong to the pain of others as to our own [18]. MLDS projects emotional arousal towards the PFC by two complementary pathways: Reward-seeking emotions are transmitted to the OFC while insecurity about the reward-seeking is transmitted to the vmPFC [19]. Sensory input which is not recognized by Hip is transmitted to the Occipital lobe by the Posterior Cingulate Cortex [20].

As the primary function of MLDS, denoted \mathbf{L} , is to serve the Reticular Activation Client (\mathbf{x}) in a complementary way, it is specified as $\mathbf{L}(\mathbf{x})$ in our model. So, $\mathbf{L}(\mathbf{x})$ represents both an internal client-server relationship resembling the CNS of other Mammals as well as a client to be served by Neocortex which is unique to man.

3.3 Parietal and Temporal Lobes as Cognitive Servers

A review of neuro-cognitive processes involved in true and false memories concludes that different neuro-cognitive processes have been linked to the formation of memories, however, most consistently the medial temporal lobe has been linked with the dlPFC [21]. The retrieval of memories from Medial Temporal Lobe by dlPFC has an independent role in the cognitive function (R_i). R_i is a coefficient of retrieval specific to domains. The complete cognitive retrieval process ($R_i c^2$) has been identified in the EEG as High-Gamma waves modulating Theta-waves mostly in the Temporal Lobe [22]. Also, an automatic dorsal pathway connecting the visual Cortex with the dlPFC by the Parietal Cortex is evidenced [23]. An EEG-study of AHA-experiences has demonstrated that the Intraparietal Sulcus (IPS) in this dorsal pathway is a visuospatial sketchpad which is central to non-prepared non-verbal insight (AHA-experiences) [24]. Also, this function is the root of numerical processing [25]. AHA-experiences represents 'stochastic' or non-verbal learning by IPS which is denoted ϵ in our model.

3.4 Neuroeconomic Model of Frontal Integration

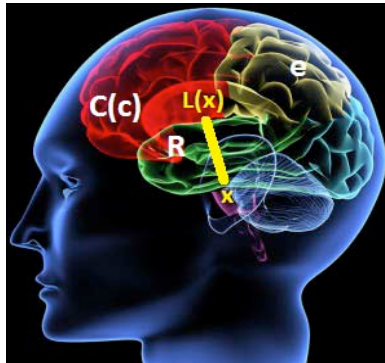


Figure 1. The review has identified two sub-systems of Frontal integration (C) with vmPFC (c) as the overlapping integrator: Firstly, a *value system* with OFC as the specialized Frontal centre controlling $L(x)$. Secondly, a *value prediction with* dlPFC as the specialized Frontal center being served by the Temporal (R_i) and Parietal (ϵ) lobes.

The neuroeconomic components interact in semantic processing in the way that the MLDS value setting ($L(x)/c$) and the Frontal value prediction complex ($R_i c$) form an antagonist equilibrium as illustrated in figure 2 [26-27]. MLDS determines the equilibrium (E) [28]. The larger baseline arousal the larger the relative dominance of emotions (MLDS) compared to cognitive (Neocortical) processes.

The dynamics of Frontal Integration (C) or general problem solving may now be formulated as a neuroeconomic model (NeM) of DM to complete formula I:

$$C = R_i c^2 / L(x) + \epsilon \rightarrow 1 \quad (2)$$

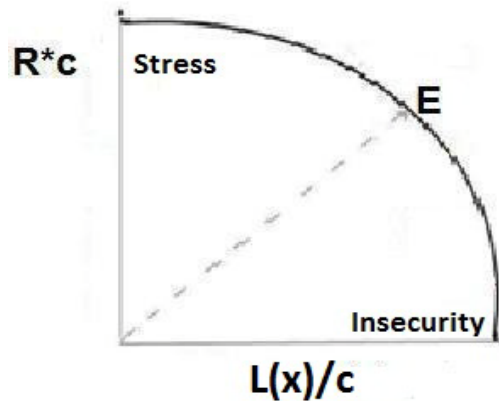


Figure 2. The state of the CNS is described by cybernetic terms: $C < 1$ is a state of under-determination or insecurity where limbic anxiety (A_m) is insufficiently stabilized by c as exemplified by anxiety-disorders e.g. post- traumatic stress disorder [29]. An emotionally stressful state indicated by the basal heart rate variability [30]. $C > 1$ is a state of over-determination or cognitive stress where the number of restrictions (equations) surmounts the number of resources (variables) giving only partial equilibrium with a low level of satisfaction. This state represents a typical male response to psychological stress with opposite effects on Frontal blood flow (CBF) in Prefrontal and Orbitofrontal Cortex as a robust response that persisted beyond the stress task period [31] and was associated with an increasing level of serum cortisol (stress hormone). $C = 1$ is an optimal state of minimal insecurity where recollected memories ($R_i c^2$) serve to stabilize limbic anxiety (A_m) without suppressing salient preferences ($L(x)$).

4 Discussion

4.1 Validation of NeM

4.1.1 Early home-supported discharge

When patients move from a hospital clinic to their own home their blood pressure declines 5-7 mmHg [32]. Following NeM such Limbic relaxation may empower the cognitive function which may be used for better rehabilitation. Actually, home-based rehabilitation is object to a number of research projects. Especially stroke patients have a large risk of severe disablement as nearly 30% may have poor outcome (PO) – dies or become disabled – by 6 months follow-up after admission.

The Cochrain Trialists have reviewed a series of RCT on Early Home-supported Discharge (EHSD) as compared to usual care for patients suffering from stroke [33]. The meta-analysis demonstrates a significant reduction in PO while traditional hospital measures as Barthél Index or Functional Independence Measure only show non-significant tendencies. In all, this indicates that the primary effect of EHSD is

rather better psychological coping than somatic training as hypothesized from NeM which is explained in figure 2 as a movement West-North on the curve from a position of $C < 1$.

4.1.2 Integrated Mind/body intervention

Physical exercise is evidenced to increase C reducing $L(x)$ while cognitive relaxation e.g. by meditation may reduce c decreasing C . Integrated programs of physical exercise and cognitive relaxation (meditation) may together expand the range of C to benefit mental health. That's the theory behind a model for an integrated mind/body approach to improved health. This model has been tested in cardiac rehabilitation during a 3-month program by 637 patients with coronary artery disease [34]. As outcome this program gave a significant improvement for patients considered to be at "higher risk" level for cardiac events.

4.2 NeM and general neural biomarkers

The neuroeconomic model of Frontal integration (Equation II) has identified two very different mental risk factors: emotional stress ($C < 1$) and cognitive stress ($C > 1$). Finding simple, reliable and valid indicators of the parameters of II may improve the diagnostics of stress and consecutively general stress-management.

4.2.1 Emotional stress

$L(x)$ is an indicator of baseline arousal which expresses some vertical conflict between MLDS and Frontal Cortex. This state has a fairly simple indicator in the basal heart rate variability [30].

4.2.2 Cognitive stress

According to [12] is the capacity of FPC that limited that is represents a major risk for overload and consecutive cognitive stress. Frontal integration aiming balance between expected and realized outcomes (Eq. II) is rooted in a complementary specialization of the Frontal Cortex where chronic dominance of the left dIPFC is demonstrated as sub-optimal for problem solving during insecurity [35]. While the right hemisphere dominates inhibitory control of emotions [36] dominates the left hemisphere facilitation of motor planning and as such goal-directed behavior [37]. According to [12] may chronic dominance of dIPFC rooted in overloaded goal-direction damage the "cognitive branching" in FPC. A fMRI of explorative versus exploitative behavior supports this concept of cognitive stress [13]. However, as MRI (BOLD) does not distinguish between inhibitory and facilitating neuroactivity, does exploitative behavior not show relative dominance of dIPFC as compared to OFC by BOLD [13].

The Frontal integrator (c) has a fairly simple indicator in the level of galvanic skin conductance (GSC) [38]. Also, GSC may differentiate between specialized hemispheric action: Visual stimuli have stronger responses in the right hemisphere while linguistic stimuli have stronger responses in the left hemisphere [39]. Further, stress rising GSC covariates with increased FPC asymmetry in the EEG in the direction of increasing dominance of the left hemisphere [40]. Does the basal GSC hand balance indicate hemispheric dominance? In order to test this hypothesis a pilot test is reported on the relative GSC hand balance of engineers (supposed to represent group dominance of the left hemisphere) and sales consultants (supposed to be more emphatic without special left hemispheric dominance). Actually, the group of engineers showed a significant left hemispheric dominance while the sales consultants did not [41]. Further, the pilot showed that dominance of the left respective the right hemisphere is asymmetrical with larger standard deviation of the right hemisphere as compared to the left hemisphere. Although these results are promising, more tests are required to conclude the basal GSC hand balance as valid indicator of cognitive stress.

5 Conclusion

This review has identified four different partitions of the Frontal Cortex which are relevant to Mesolimbic dopamine activity ($L(x)$) by control of OFC and activation of cognitive analysis by dlPFC in order to maintain long term goals in the FPC (C). The cognitive analysis is served by semantic memories recalled from the Temporal Lobe (R_i) and a visuospatial sketchpad in the Parietal Lobe (ϵ). This neuroeconomic model of Frontal integration (NeM) has the following form:

$$C = R_i c^2 / L(x) + \epsilon \rightarrow 1 \quad (3)$$

NeM explains the core effect of integrated homecare e.g. for stroke patients as improved coping arising from better Limbic relaxation at home. Further, NeM distinguishes between emotional and cognitive stress related to Limbic and Frontal systems, respectively. Emotional stress ($C < 1$) is rooted in vertical conflict between MLDS and Frontal Cortex as indicated by the basal heart rate variability; Cognitive stress ($C > 1$) is rooted in overloaded goal-direction by dlPFC as indicated by the galvanic skin conductance balance of hands. Further research may focus how the general neural biomarkers relate to an established stress marker as plasma cortisol.

As model construct to identify general neural biomarkers NeM may be seen as a synthesis of the triune models of McLean [1] and Luria [2]. This synthesis is a quadriune model where the two lower levels of the McLeanian model (Reptile brain stem and Mammalian midbrain (including Cingulate Cortex) as $L(x)$) interact with the two higher levels of the Lurian model (Frontal executive (c^2), Temporal memory (R_i) and Parietal visuospatial sketchpad (ϵ)). Further, NeM elaborates the triadic model of

Ernst [4] explaining the core function of vmPFC as simultaneous control of emotions by OFC and predictive recollection of memories by dlPFC with a view to a pending long term goal in FPC. Finally, the cognitive stress model of Koechlin and Hyafil [12] is combined with the post-traumatic stress model of Bremner [29] which leads to the identification of two very different general stress syndromes with relatively simple biomarkers.

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