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Regaining Cognitive Control: An Adaptive Computational Model Involving Neural Correlates of Stress, Control and Intervention

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Abstract. Apart from various other neural and hormonal changes caused by stress, frequent and long-term activation of the hypothalamus–pituitary–adrenal (HPA) axis in response to stress leads in an adaptive manner to the inadequacy of the stress response system. This leads to a cognitive dysfunction where the subject is no more able to downregulate his or her stress due to the atrophy in the hippocampus and hypertrophy in the amygdala. These atrophies can be dealt with by antidepressant treatment or psychological treatments like cognitive and behavioural therapies. In this paper, an adaptive neuroscience-based computational network model is introduced which demonstrates such a cognitive dysfunction due to a long-term stressor and regaining of the cognitive abilities through a cognitive-behavioural therapy: Mindfulness-Based Cognitive Therapy (MBCT). Simulation results are reported for the model which demonstrates the adaptivity as well as the dynamic interaction of the involved brain areas in the phenomenon.

Keywords: Stress induced neural anatomy · Negative metaplasticity · Mindfulness · Adaptive causal modeling · Cognition · Positive metaplasticity · Therapy

1 Introduction

Alteration in cognitive abilities can, potentially, be caused by the various ups and downs in humans' life and body. For instance, although termed to vary person to person, decline in cognitive abilities with increasing age and long-term stress have been confirmed by [1, 2]. Similarly, another discrepancy in the cognitive abilities is the lack of flexibility with age [3] which is considered very essential by many, specifically in changing situations. Taking the potentially negative consequences of long-term stress into account, various studies have reported similar findings regarding its effects in the long run [2, 4, 5], i.e., cognitive decline. At the cellular level, according to [6, 7], the cell loss and, therefore, changes in the synaptic plasticity take place because of the decrease in the brain-derived neurotrophic factor (BDNF) caused by the increase in the glucocorticoids.

To handle this severe problem in cognition, various studies, for instance [2], suggest antidepressant treatment but on the other hand, [8, 9] come up with Mindfulness-Based Cognitive Therapy (MBCT) [10] as an effective treatment for similar problems in general

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and cognitive impairments caused by long-term stress. In MBCT, the subject is trained to focus on the present moment, gain awareness of himself and accept reality. Cognitive Behaviour Therapy (CBT) is another, almost similar therapy but according to [11] MBCT was found more effective when compared to CBT and that's also the reason why the study presented here considers MBCT. The reason may lie in the fact that the later combines techniques from the former with a mindfulness training program which provides added value.

Moreover, to combine these concepts into a single model, this study considers an adaptive network modeling approach [12] because of its efficacy and suitability for the adaptive and cyclic processes, as demonstrated in [13, 14]. In rest of the paper, Sect. 2 gives brief account of the literature on the subject, Sect. 3 presents the adaptive network model, which is explained by simulation results in detail in Sect. 4. Finally, the paper is concluded in Sect. 5.

2 Related Work

The alteration in cognitive abilities caused by long-term stress are attributed to the neuronal losses at the cellular level caused by stress. These changes are considered similar to those caused by depression [2]. For instance [6] links such cellular changes in the hippocampus to the increased level of glucocorticoid hormones, i.e., cortisol. Similarly, at the molecular level too, these cellular paucities were found in the hippocampus which are, most of the time, caused by the decrease expression of BDNF and resultant increased level of glucocorticoid/cortisol [6, 7, 15]. The down-regulating role of the increased level of glucocorticoids in the hippocampal expression has also been reported by [16]. BDNF is considered essential for neuronal survival, but [17] attributes reduction of BDNF to the potential mediating action of glucocorticoid on the hippocampus.

The effect of the boost of glucocorticoids is referred to as negative metaplasticity as it downregulates adaptivity of the hippocampal synaptic connectivity. In contrast, the boost in the expression of BDNF is referred to as positive metaplasticity as it strengthens connectivity in the hippocampus. These changes in the background, at the neural level, cause lack of control at the forefront or what we know as cognitive loss whereby the subject lacks the ability to regulate his or her emotions in an adaptive manner. Having said this, it is also possible that the same process is reversed by adequate means (antidepressant treatment for instance [2]), increasing the expression of BDNF. Synapses process and transmit neural information with some efficacy. Alteration in the synapsis is called synaptic plasticity or (first-order) synaptic adaptation. As mentioned above, synaptic plasticity itself can also change which is referred to as second-order adaptation or metaplasticity. According to [2], if metaplasticity improves the adaptive cognitive function, it's considered positive metaplasticity but on the contrary, if it brings impairment to the aforementioned adaptive cognitive function then it's called negative metaplasticity. This kind of cognitive impairment has been observed in both humans [18] and animals [19] as a result of long-term stress [20, 21].

MBCT, that is modeled here as a treatment for the above cognitive deficit, is considered a very effective approach [8, 9]. This therapy improves psychological health by increasing mindfulness. It combines Kabat-Zinn's [10] mindfulness-based stress reduction program with the techniques used in CBT. MBCT, therefore, promotes acceptance of

feelings without judgement, focusing on the present moment and awareness of self [22]. Acceptance enables the person to disintegrate him or herself from the negative thoughts and consider emotions as a non-permanent event [23]. After this disengagement from negative thoughts, the mindfulness training helps the person in positive reappraisal [24]. Similarly, the focus on the present moment helps the person get insight of his or her own feelings and sensations for successful reappraisal of his thoughts. Generally, there are various brain areas involved in all these processes of MBCT but the most responsible parts that are considered essential for successful MBCT are the anterior cingulate cortex (ACC), insula, temporo-parietal junction, posterior cingulate cortex and prefrontal cortex (PFC) [15]. Activation of ACC helps enhance attention regulation by sustaining attention on a chosen object. Insula and temporo-parietal junction enhance body awareness by focusing on the internal experience like emotions, breathing and body sensation. PFC is responsible for the control of emotion regulation. Moreover, PFC together with posterior cingulate cortex, insula, temporo-parietal junction also helps the person change his perspective on himself [15].

Currently, there are various modeling techniques used in the field of artificial intelligence, specifically for modeling and simulating brain processes as summarized in [25, 26] but this study uses [12] because of its suitability for the model presented in this paper. This modeling approach comes under the umbrella of causal modeling which has a long history in Artificial Intelligence, e.g., [27, 28]. The dynamic and adaptive perspective on causal relations makes this technique unique among other similar approaches. Here, causal effects are exerted over time. Interestingly, the causal relations themselves are adaptive and can change over time too. Moreover, this type of adaptation can itself be adaptive too, leading to second-order adaptivity as occurs in metaplasticity; e.g., [2]. The network model introduced here is a *second-order adaptive temporal-causal network model* whereby adding dynamics and adaptation makes the model capable of application that would otherwise be out of scope of the causal modeling. This provides us with a useful opportunity to transform qualitative processes as described in empirical literature into adaptive causal network models. Simulations then can show that the underlying neural mechanisms that according to the assumptions made in this empirical literature explain certain observed emerging phenomena are indeed able to generate the phenomena computationally.

3 Multilevel Adaptive Cognitive Modeling

The multilevel adaptive causal network modeling approach [12, 29] has been used as a tool for the development and simulation of the adaptive causal model. The conceptual and numerical representation of the network characteristics used are summarized below in Table 1. Currently, this technique provides a dedicated software environment with a library of over 40 combination functions, publically available at https://www.researchgate.net/publication/336681331, for combining the incoming causal impacts to a network state. The library also includes facilities to compose the existing functions into new functions by mathematical function composition. Moreover, self-defined functions can also be added to the library easily as per need of the model and phenomenon which makes this technique very feasible and flexible. The combination functions used in the current paper are shown in Table 2.

Table 1. Conceptual and numerical representations of the network characteristics used

Concept	Conceptual representation	Explanation
Connectivity characteristics		
States and connections	X, Y, $X \rightarrow Y$	Describes the nodes (representing state variables, shortly called *states*) and links (representing causal *connections* between states) of the network
Connection weight	$\boldsymbol{\omega}_{X,Y}$	A *connection weight* $\boldsymbol{\omega}_{X,Y}$ (usually in $[-1, 1]$) represents the strength of the causal impact of state X on state Y through connection $X \rightarrow Y$
Aggregation characteristics		
Aggregating multiple impacts on a state	$\mathbf{c}_Y(..)$	For each state Y (a reference to) a *combination function* $\mathbf{c}_Y(..)$ is chosen to combine the causal impacts of other states on state Y
Timing characteristics		
Timing of the effect of causal impact	$\boldsymbol{\eta}_Y$	For each state Y a *speed factor* $\boldsymbol{\eta}_Y \geq 0$ is used to represent how fast a state is changing upon causal impact
Concept	**Numerical representation**	**Explanation**
State values over time t	$Y(t)$	At each time point t each state Y in the model has a real number value, usually in [0, 1]
Single causal impact	$\mathbf{impact}_{X,Y}(t) = \boldsymbol{\omega}_{X,Y} X(t)$	At t state X with a connection to state Y has an impact on Y, using connection weight $\boldsymbol{\omega}_{X,Y}$
Aggregating multiple causal impacts	$\mathbf{aggimpact}_Y(t) = \mathbf{c}_Y(\mathbf{impact}_{X1,Y}(t),\ldots, \mathbf{impact}_{Xk,Y}(t)) = \mathbf{c}_Y(\boldsymbol{\omega}_{X1,Y} X_1(t), \ldots, \boldsymbol{\omega}_{Xk,Y} X_k(t))$	The aggregated causal impact of multiple states X_i on Y at t, is determined using combination function $\mathbf{c}_Y(..)$
Timing of the causal effect	$Y(t + \Delta t) = Y(t) + \boldsymbol{\eta}_Y\ [\mathbf{aggimpact}_Y(t) - Y(t)]\ \Delta t = Y(t) + \boldsymbol{\eta}_Y\ [\mathbf{c}_Y(\boldsymbol{\omega}_{X1,Y} X_1(t), \ldots, \boldsymbol{\omega}_{Xk,Y} X_k(t)) - Y(t)]\ \Delta t$	The causal impact on Y is exerted over time gradually, using speed factor $\boldsymbol{\eta}_Y$; here the X_i are all states with outgoing connections to state Y

Using this technique, we propose an adaptive causal network model with connectivity as given in Fig. 1. A description of the various states of the model is provided in Table 3 where the background colors differentiate between the different levels of the model. The base level refers to the basic functioning of the model, involving the regulation of the negative emotions.

Table 2. Basic combination functions from the library used in the presented model

	Notation	Formula	Parameters
Advanced logistic sum	$\mathbf{alogistic}_{\sigma,\tau}(V_1, \ldots, V_k)$	$[\frac{1}{1+e^{-\sigma(V_1+\cdots+V_k-\tau)}} - \frac{1}{1+e^{\sigma\tau}}](1+e^{-\sigma\tau})$	Steepness $\sigma > 0$ Excitability threshold τ
Hebbian learning	$\mathbf{hebb}_{\mu}(V_1, V_2, W)$	$V_1V_2(1-W)+W$	Persistence factor $\mu > 0$
Identity	$\mathbf{id}(V)$	$\mathbf{id}(V) = V$	

The first-order adaptation levels of the model explicitly represent weights $\omega_{X,Y}$ of some of the connections in the base model by *first-order self-model* states $\mathbf{W}_{X,Y}$ (also called *reification states*). For instance, $\boldsymbol{X}_{13}$ and $\boldsymbol{X}_{14}$ are first-order self-model states representing the adaptive connection weights $\omega_{\text{adrenalcortex,hippocampus}}$ and $\omega_{\text{adrenalcortex,PFC,}}$ i.e., the connections represented by the two outgoing light-blue colored arrows from$\boldsymbol{X}_6$, in the base model, respectively. The persistence μ and speed factors η of these connections' adaptation states $\boldsymbol{X}_{13}$ and $\boldsymbol{X}_{14}$ are represented by *second-order self-model states* $\boldsymbol{X}_{15}$ ($\mathbf{M}_{cortisol-feedback}$), $\boldsymbol{X}_{16}$ ($\mathbf{H}_{cortisol-feedback}$) and $\boldsymbol{X}_{17}$ ($\mathbf{M}_{cortisol}$), $\boldsymbol{X}_{18}$($\mathbf{H}_{cortisol}$), respectively. The impact of these self-modeling states on their respective states in the lower order is represented by the red downward connections from the upper levels to the lower levels.

Table 3. States and their explanation

States		Role in the model	Level
X_1	stimulus	Anything causing stress in the real world	Base Level
X_2	thalamus	Processing of sensory information	
X_3	amygdala	Detects negative emotions and informs HPA to respond [15]	
X_4	hypothalamus	Also called HPA axis: Part of autonomic stress response system which releases cortisol in the body to handle the situation [30].	
X_5	anterior-pituitary		
X_6	adrenal-cortex		
X_7	hippocampus	Memory formation [15]	
X_8	PFC	Regulator of the emotions [15]	
X_9	ACC	Activated by MBCT where: - ACC regulates attention, - Insula together with temporo-parietal-junction gives body awareness, - PFC, posterior cingulate cortex, insula and temporo-parietal junction helps in changing one's perspective on the self [15].	
X_{10}	insula		
X_{11}	temporo-parietal-junction		
X_{12}	posterior-cingulate-cortex		
X_{13}	$\mathbf{W}_{\text{cortisol-feedback}}$	First-order self-model states for hebbian learning representing connection weights $\omega_{\text{adrenalcortex,hippocampus}}$ and $\omega_{\text{adrenalcortex,PFC}}$	First-Order Self-Model Level
X_{14}	$\mathbf{W}_{\text{cortisol}}$		
X_{15}	$\mathbf{M}_{\text{cortisol-feedback}}$	These states represent the adaptive control of plasticity, also called metaplasticity as described for instance in [2, 4, 5]. The hormones released by HPA which can cause negative as well as positive metaplasticity in different brain parts [30]	Second-Order Self-Model Level
X_{16}	$\mathbf{H}_{\text{cortisol-feedback}}$		
X_{17}	$\mathbf{M}_{\text{cortisol}}$		
X_{18}	$\mathbf{H}_{\text{cortisol}}$		

Generally, there are various adaptive connections in the brain, the plasticity and metaplasticity of which are subject to various factors, for instance reward is one of those factors to be mentioned [31]. This model is however motivated by the psychological computational model presented in [32] but the network in this model is modeled based on anatomical knowledge in the light of the findings from neurosciences as presented in Sect. 2. This model, therefore, only considers the aforementioned two adaptive connections out of the many adaptive connections in the brain. It demonstrates the phenomenon of negative and positive metaplasticity at a neural level where long-term stress causes cognitive loss through negative metaplasticity whereby the person loses control on regulation capabilities. As a treatment, MBCT has been used in the model which enables the person to regain his or her cognitive control through positive metaplasticity. The base model is a network of main parts of human brain and body involved in the stress experiences and the MBCT. The first-order adaptation represents the hormonal changes taking place as a result of stress and its treatment i.e. MBCT. The first-order adaptation uses a Hebbian learning principle [33]. The second-order adaptation represents the adaptation of the first-order adaptation to control the adaptation.

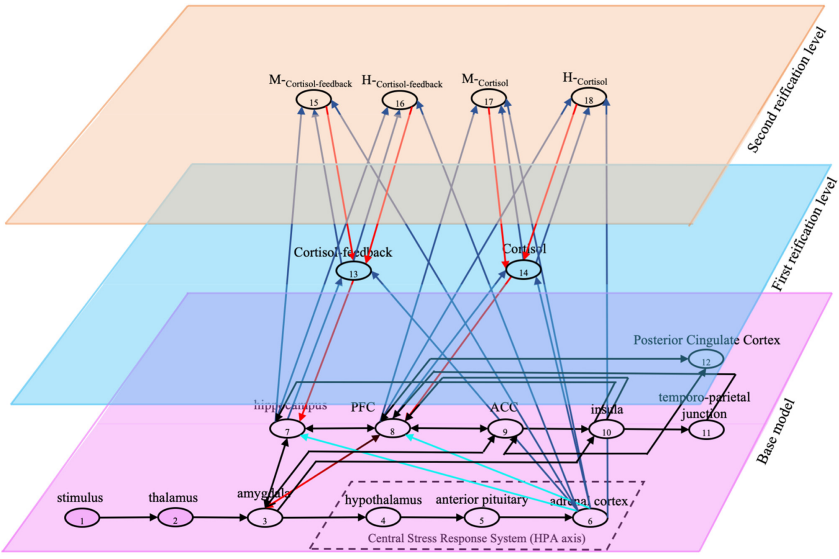


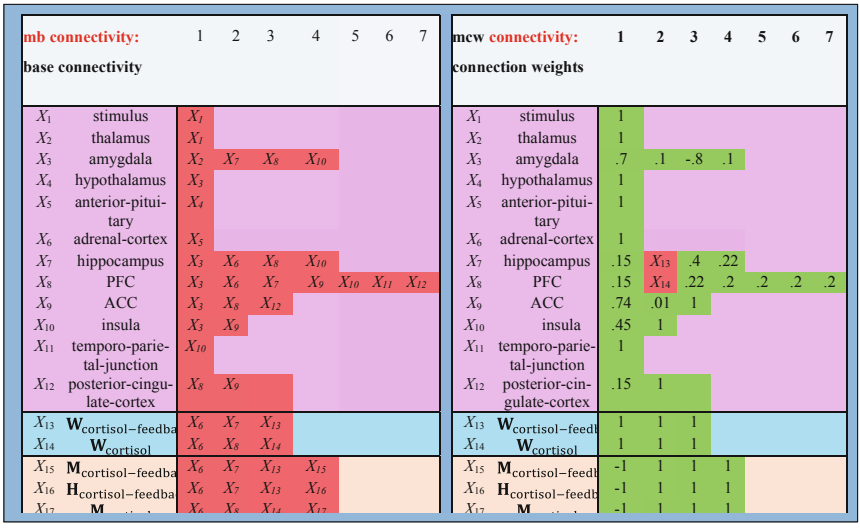
Fig. 1. Adaptive causal network model for therapeutic intervention for long-term stress

In the base model when the person faces some negative stressing stimulus, it's detected by the amygdala through the thalamus. Detection of stress by the amygdala automatically activates the Stress Response System which means activation of the Hypothalamic-pituitary-adrenal (HPA) axis as a result [30, 34]. The HPA releases cortisol to handle the situation. This works fine if this is not very frequent but repeated and prolonged activation of the HPA axis and hence prolonged release of cortisol blunts the stress response system; this is where the problem begins. In the model, the connections to PFC and hippocampus from the HPA model the hormonal effect of HPA on the two,

which impairs the function of the PFC and hippocampus leading to the lack of cognitive control called negative metaplasticity, as mentioned.

The MBCT practice, on the other hand, activates the ACC, insula, temporo-parietal junction and posterior cingulate cortex which helps the person decrease activation of the HPA and hence less release of cortisol over time [15]. At the neural level these changes are considered as positive metaplasticity as the person regains control over his cognitive abilities. The **M-** and **H-**states represent the persistence and speed factor of the learning taking place at the respective base level connections.

In Box 1 and Box 2, the full specification of the network characteristics needed for reproduction of the model results are given. These specifications are not only essential for the reproduction of the results demonstrated in Fig. 2, 3, 4 and 5 but also qualitatively validates the model against the relevant literature in the sense that they show that personal characteristics exist by which indeed the assumed neural mechanisms lead to the overall patterns reported in the literature. Box 1 contains the connectivity role matrices called **mb** and **mcw**. Here **mb** gives all those incoming connection to a state which are either at the same level or from a lower level. The downward connections are indicated in role matrix **mcw** wherein they are used as indicator of their respective adaptive connection. For instance, in the model in Fig. 1, state X_{13} (i.e., a **W**-state) represents the adaptive base level connection from X_6 to X_7, the causal effect of which is modeled by the downward connection from X_{13} to X_7. Similarly, the adaptive connection from X_6 to X_8 is represented by X_{14} showing the cortisol level, the frequent and increased expression of which causes cognitive loss.



mb connectivity: base connectivity

		1	2	3	4	5	6	7
X_1	stimulus	X_1						
X_2	thalamus	X_1						
X_3	amygdala	X_2	X_7	X_8	X_{10}			
X_4	hypothalamus	X_3						
X_5	anterior-pituitary	X_4						
X_6	adrenal-cortex	X_5						
X_7	hippocampus	X_3	X_6	X_8	X_{10}			
X_8	PFC	X_3	X_6	X_7	X_9	X_{10}	X_{11}	X_{12}
X_9	ACC	X_3	X_8	X_{12}				
X_{10}	insula	X_3	X_9					
X_{11}	temporo-parietal-junction	X_{10}						
X_{12}	posterior-cingulate-cortex	X_8	X_9					
X_{13}	$\mathbf{W}_{\text{cortisol-feedba}}$	X_6	X_7	X_{13}				
X_{14}	$\mathbf{W}_{\text{cortisol}}$	X_6	X_8	X_{14}				
X_{15}	$\mathbf{M}_{\text{cortisol-feedba}}$	X_6	X_7	X_{13}	X_{15}			
X_{16}	$\mathbf{H}_{\text{cortisol-feedba}}$	X_6	X_7	X_{13}	X_{16}			
X_{17}	**M**	X_6	X_8	X_{14}	X_{17}			

mcw connectivity: connection weights

		1	2	3	4	5	6	7
X_1	stimulus	1						
X_2	thalamus	1						
X_3	amygdala	.7	.1	-.8	.1			
X_4	hypothalamus	1						
X_5	anterior-pituitary	1						
X_6	adrenal-cortex	1						
X_7	hippocampus	.15	X_{13}	.4	.22			
X_8	PFC	.15	X_{14}	.22	.2	.2	.2	.2
X_9	ACC	.74	.01	1				
X_{10}	insula	.45	1					
X_{11}	temporo-parietal-junction	1						
X_{12}	posterior-cingulate-cortex	.15	1					
X_{13}	$\mathbf{W}_{\text{cortisol-feedl}}$	1	1	1				
X_{14}	$\mathbf{W}_{\text{cortisol}}$	1	1	1				
X_{15}	$\mathbf{M}_{\text{cortisol-feedl}}$	-1	1	1	1			
X_{16}	$\mathbf{H}_{\text{cortisol-feedl}}$	-1	1	1	1			
X_{17}	**M**	-1	1	1	1			

Box 1. Role matrices for connectivity characteristics.

Similarly, role matrices **mcfw**, **mcfp** for the aggregation characteristics and **ms** for the timing characteristics are given in **Box** 2. Matrix **mcfw** contains selection of the combination functions used for aggregation of the incoming causal impact at a state X_i.

For instance, state X_8 uses **alogistic(..)** and state X_{14} uses **hebb(..)** combination function as given in Table 2. Moreover, the first-order adaptation state X_{18} uses the Hebbian learning combination function **hebb(..)** from the same table. Role matrix **mcfp** specifies the parameter values for each of the combination function as indicated in **mcfw**. Note here that the red cells with numbered state names X_i in it, indicate the downward connections from these states in all the matrices except **mb**. Role matrix **ms** carries all the speed factor values of the states. In role matrix **ms**, the rows with red cells represent the state with adaptive speed factors i.e. X_{13} and X_{14}.

mcfw	aggregation:	1	2	3
Combination function weights		alogistic	hebb	Id
X_1	stimulus			1
X_2	thalamus			1
X_3	amygdala	1		
X_4	hypothalamus			1
X_5	anterior-pituitary			1
X_6	adrenal-cortex			1
X_7	hippocampus	1		
X_8	PFC	1		
X_9	ACC	1		
X_{10}	insula	1		
X_{11}	temporo-parietal-junction	1		
X_{12}	posterior-cingulate-cortex	1		
X_{13}	$\mathbf{W}_{cortisol-feed}$		1	
X_{14}	$\mathbf{W}_{cortisol}$		1	
X_{15}	$\mathbf{M}_{cortisol-feedb}$	1		
X_{16}	$\mathbf{H}_{cortisol-feedb}$	1		
X_{17}	$\mathbf{M}_{cortisol}$	1		
X_{18}	$\mathbf{H}_{cortisol}$	1		

mcfp	aggregation	1		2	3
Combination function parameters		Alogistic σ	τ	Hebb μ	id
X_1	stimulus				1
X_2	thalamus				1
X_3	amygdala	8	.4		
X_4	hypothalamus				1
X_5	anterior-pituitary				1
X_6	adrenal-cortex				1
X_7	hippocampus	8	.52		
X_8	PFC	8	.56		
X_9	ACC	18	.69		
X_{10}	insula	18	.64		
X_{11}	temporo-parietal-junction	18	.6		
X_{12}	posterior-cingulate-cortex	18	.4		
X_{13}	$\mathbf{W}_{cortisol-feedba}$			X_{15}	
X_{14}	$\mathbf{W}_{cortisol}$			X_{17}	
X_{15}	$\mathbf{M}_{cortisol-feedba}$	10	.91		
X_{16}	$\mathbf{H}_{cortisol-feedba}$	10	1.05		
X_{17}	$\mathbf{M}_{cortisol}$	10	.75		
X_{18}	$\mathbf{H}_{cortisol}$	10	.75		

ms timing:		1
		Speed factors
X_1	stimulus	0
X_2	thalamus	1
X_3	amygdala	.2
X_4	hypothalamus	.3
X_5	anterior-pituitary	.3
X_6	adrenal-cortex	.3
X_7	hippocampus	.3
X_8	PFC	.2
X_9	ACC	.01
X_{10}	insula	.015
X_{11}	temporo-parietal-junction	.01
X_{12}	posterior-cingulate-cortex	.015
X_{13}	$\mathbf{W}_{cortisol-fee}$	X_{16}
X_{14}	$\mathbf{W}_{cortisol}$	X_{18}
X_{15}	$\mathbf{M}_{cortisol-fee}$	0.01
X_{16}	$\mathbf{H}_{cortisol-fee}$	0.01
X_{17}	$\mathbf{M}_{cortisol}$	0.01
X_{18}	$\mathbf{H}_{cortisol}$	0.01

Box 2. Role matrices for aggregation and timing characteristics

4 Simulation Results

Simulation results for an example scenario are provided here with and without MBCT, which shows how a person can go into a complete loss of cognitive abilities (caused by long-term stress) contrary to recovery from the cognitive loss. The results can be obtained by providing the values given in Box 1 and Box 2 to the dedicated software as mentioned above with the initial values of the states as shown in Table 4.

Figure 2 demonstrates the effect of long-term stress at the neural level where frequent and long-term expression of the cortisol by HPA blunts the autonomic stress response system. It can be seen that initially when the amygdala gets activated by some kind of

Table 4. Initial values of the states

State	Stimulus	All other base states	Cortisol-feedback (**W**)	Cortisol (**W**)	$\mathbf{M}_{\text{Cortisol}-\text{feedback}}$	$\mathbf{H}_{\text{Cortisol}-\text{feedback}}$	$\mathbf{M}_{\text{Cortisol}}$	$\mathbf{H}_{\text{Cortisol}}$
Value	1	0	0.3	0.3	0.5	0.9	0.5	0.9

stressful event, the hippocampus and PFC also gets activated which helps in activating the associated memory and handling of the stress respectively. But as this goes longer, the person's hippocampus and PFC are no longer activated despite the fact that the amygdala and the HPA are still very high.

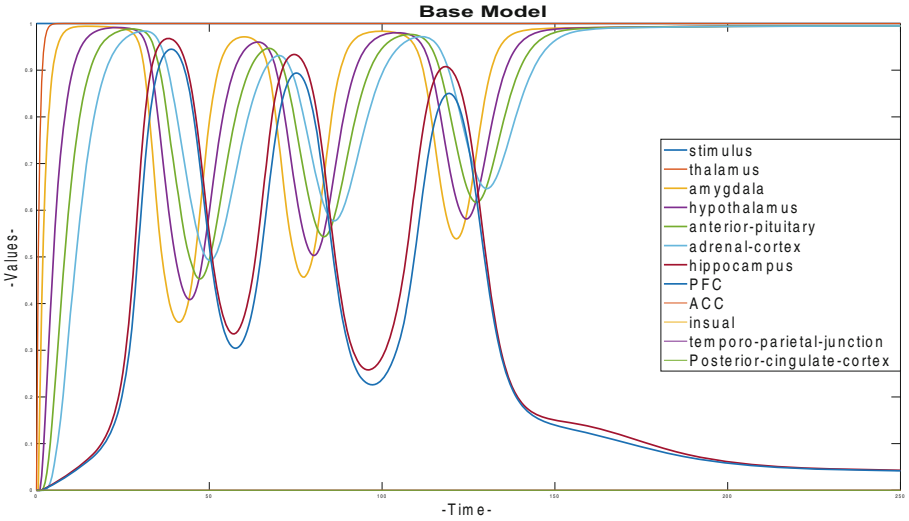


Fig. 2. Base model without therapy

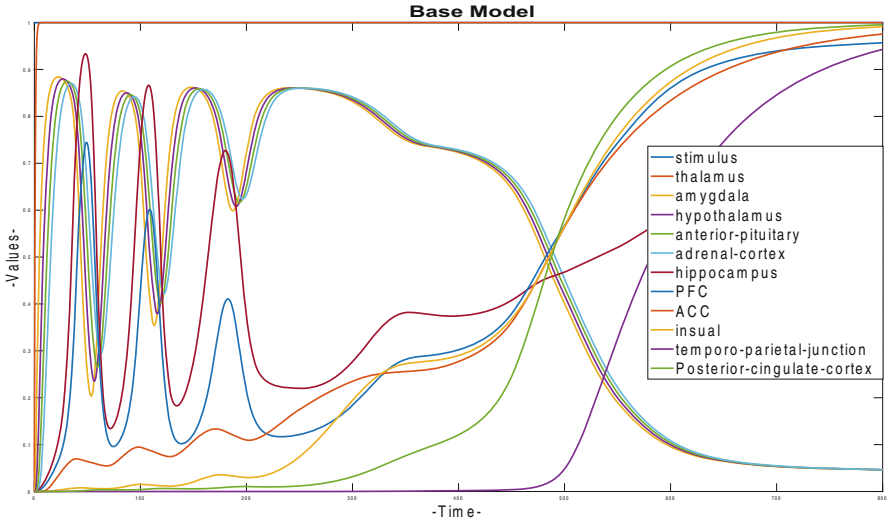


Fig. 3. Base model with therapy

Contrary to Fig. 2, in Fig. 3 it can be seen that although the person's cognitive abilities go down for some period, this doesn't remain like this for longer. It's because the person

undergoes the proposed therapy which helps the person slowly regain his cognitive abilities. The therapy, on one hand makes the person not get stressed so easily and on the other hand it decreases the activation of HPA and hence expression of cortisol which has positive plastic and metaplastic effects on the Hippocampus and PFC. Therefore, both of these important parts of the brain start functioning as normal and regulate the negative stress the person is facing. At the neural level, this happens because in the MBCT, the person activates his or her other brain parts like ACC, insula, temporo-parietal-junction and posterior-cingulate-cortex which helps the person regulate his attention, get awareness of himself and change his perspective about himself, respectively.

In connection to Fig. 2 above, Fig. 4 shows the first- and second-order adaptation. Cortisol-feedback shows the Hebbian learning taking place at the connection in the base level between the HPA and hippocampus wherein impairment takes place at the hippocampus due to the increase level of cortisol. These states in the first-order adaptation level are the **W-**states. Similarly, the cortisol represents the second **W-**state which represent the learning taking place at the connection in base level between HPA and PFC. Moreover, the two **M-** and **H-**states represent the persistence and speed factor of the negative plasticity here, for metaplasticity. As this figure only shows the negative plasticity, therefore these connections only decrease, representing cognitive loss.

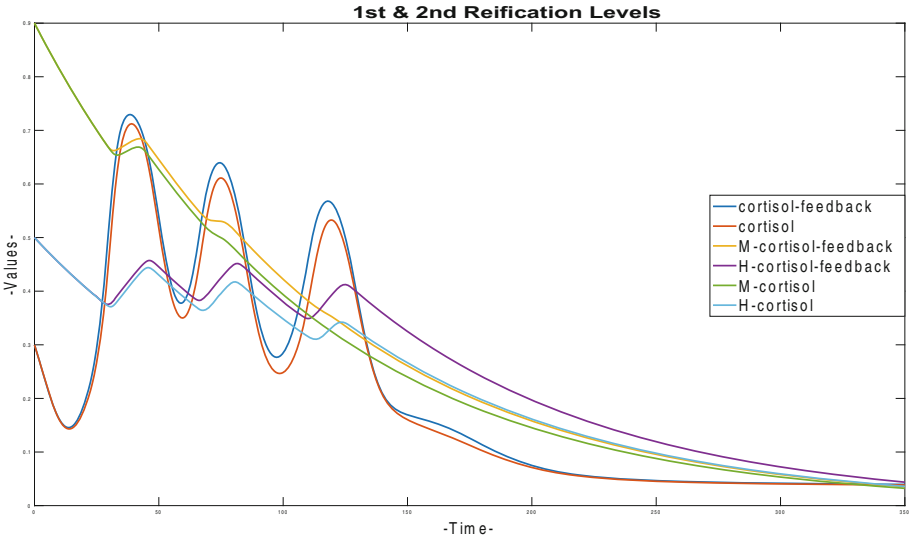


Fig. 4. First and second-order self-model states indicating negative plasticity and metaplasticity

Figure 5 in connection to Fig. 3 shows negative as well as positive metaplasticity. As already explained above, initially negative plasticity is taking place because of the excessive expression of the cortisol but when the person starts MBCT training, the situation starts getting reversed. Initially the person reverses the learning as can be seen that the cortisol-feedback and cortisol (the learning taking place at the HPA to hippocampus and PFC connections respectively) starts getting increasing. While the **M-** and **H-**states increasing slowly representing the persistence and speed factor of the

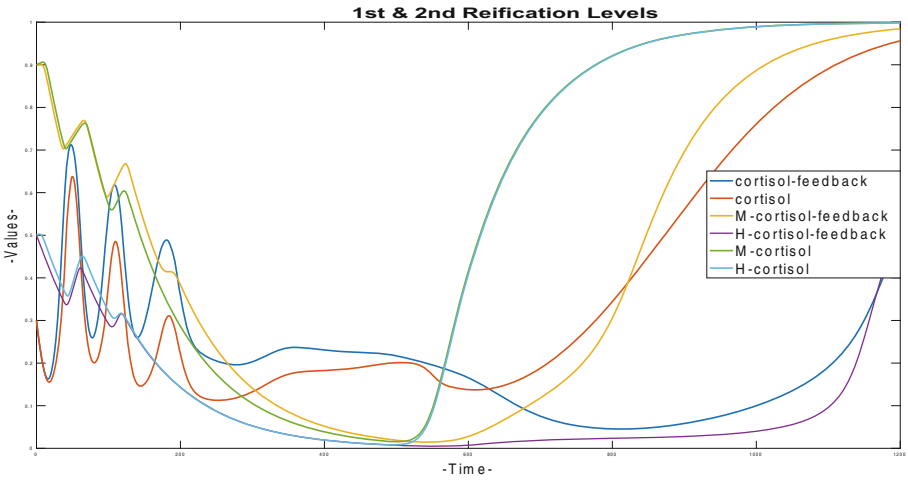


Fig. 5. First and second-order self-model states indicating negative and positive plasticity and metaplasticity

learning taking place called positive metaplasticity. These changes show it effect in the form of normal activation of the hippocampus and PFC in response to stress as discussed in Fig. 3 above.

5 Conclusion

The introduced adaptive network model is based on the neural correlates of stress response system and MBCT. It was designed using a multilevel adaptive network-oriented causal modeling approach in such a way that the anatomy of stress and MBCT induced brain parts were incorporated. The concepts of plasticity and metaplasticity have a long history in neuroscience. The model demonstrates the processes through simulations, showing how negative and positive metaplasticity occur with their effects on health. These results can be made as close to available empirical data as possible. This can also prove as a base for virtual training agent for therapies. The implementation of these techniques in the way done in this paper through the multilevel adaptive causal network model makes these processes easily understandable but also makes it an easy choice for implementation in the form of a complex artificially intelligent systems to work in a human-like manner.

During this study, it was learnt that, although quite a lot of work has been done in these areas of neuroscience, the anatomy of these processes, specifically in case of the aforementioned therapy are still not fully clear. Therefore, a temporal anatomy of the brain parts activated by such therapies would be a valuable contribution. This will not only make it easier to understand the flow of these complex processes going on in the brain but also make its implementation feasible in a more realistic way.

Apart from the added values of the model to neuroscience research, this paper also acknowledges the scope of causal modeling e.g., [27, 28] which has gotten even wider

with the dynamicity brought by the multi-order adaptation [12, 29] as it has enabled this modeling approach to model phenomenon that would otherwise be not possible. In the future, the authors aim at developing a virtual agent system for training based on this model where the agent would collect data from body sensors of the patient and help him in undergoing therapies accordingly.

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