Integrative Cognitive and Affective Modeling of Deep Brain Stimulation

Seyed Sahand Mohammadi Ziabari(✉)

Social AI Group, Vrije Universiteit Amsterdam, De Boelelaan 1105,
Amsterdam, The Netherlands
sahandmohammadiziabari@gmail.com

Abstract. In this paper a computational model of Deep Brain Stimulation (DBS) therapy for post-traumatic stress disorder is presented. The considered therapy has as a goal to decrease the stress level of a stressed individual by using electrode which placed in a specific area in brain. Several areas in brain have been used to decrease the stress level, one of them is Amygdala. The presented temporal-causal network model aims at integrative modeling a Deep Brain Stimulation therapy where the relevant brain areas are modeled in a dynamic manner.

Keywords: Deep Brain Stimulation · Amygdala · Network-Oriented Modeling · PTSD

1 Introduction

Post-Traumatic Stress Disorder (briefly PTSD) [15] is a severe psychiatric mental problem that might happen in an individual after serious trauma or extreme stress. PTSD can generate intense apprehension, impuissance in persons [1]. It has been known that electrical stimulation of the amygdala has a remarkable effect and changes on emotional, perceptual, and behavioral functioning.

What is deep brain stimulation is completely explained in [6, p. 406, 12]:

> ‘The implementation of DBS electrodes is a neurosurgical procedure, often performed under local anesthesia with patients fully awake to facilitate precise stimulation mapping. After placement of the electrodes in the desired target below the convexity of the brain, they are connected to a programmable pulse generator, similar to modern cardiac pacemakers, that is implanted under the skin below the collarbone.’

There are variety of indications for PTSD such as insomnia, hypervigilance, and stress [14]. Some brain components are involved in having reaction to the stress like cerebral Cortex, Hippocampus, Hypothalamus, Amygdala [12]. The Network-Oriented Modeling approach based on temporal-causal network models described in [16] is such a modeling approach, and has been used here.

The paper is organized as follows. In Sect. 2 the underlying biological and neurological principles concerning the parts of the brain involved in stress and in the suppression of stress are addressed. In Sect. 3 the integrative temporal-causal network model is introduced. In Sect. 4 simulation results of the model are discussed, and eventually in the last section a conclusion is presented.

F. Wotawa et al. (Eds.): IEA/AIE 2019, LNAI 11606, pp. 608–615, 2019.
https://doi.org/10.1007/978-3-030-22999-3_52

2 Underlying Biological and Neurological Principles

As have been discussed in the literature a deep brain stimulation (DBS) has an important role in treatment with PTSD; e.g., [1]. There are many other therapies which have been explained in [18–27]. For instance, the cognitive models of using Ritalin and doing yoga to decrease the stress level presented in [24] and [25], respectively. The efficiency of deep brain stimulation and also the method is introduced precisely in [1, p. 1]:

> 'Deep Brain Stimulation (DBS) has shown promise in refractory movement disorders, depression and obsessive-compulsive disorder, with deep brain targets chosen by integration of clinical and neuroimaging literature. The basolateral amygdala (BLn) is an optimal target for high-frequency DBS in PTSD based on neurocircuitry findings from a variety of perspective.'
> 'An electroencephalographic [EEG] telemetry session will test safety of stimulation before randomization to staggered-onset, double-blind sham versus active stimulation for two months.'
> 'Deep Brain Stimulation (DBS) refers to the process of delivering an electrical current to a precise location in the brain. DBS is now a common clinical practice. DBS is an invasive treatment, and the potential for benefits must clearly outweigh the risks.'

It notable that only stimulation of the BLn [11] has remarkable effect on curing PTSD as stated in [1, p. 7]:

> 'DBS of gray matter, such as the BLn, would likely have effects opposite those seen from DBS of the white matters in the case of the amygdala.
>
> 1. It supports the model that amygdala overactivity is responsible for the symptoms of PTSD. DBS of the stria terminals physiologically equates to amygdala overactivity. In this patient with no psychiatric history, an increase in amygdala output activity has led to symptoms commonly seen in combat PTSD (for example, irritability, helplessness, depression and suicidality.)
> 2. The correction of the amygdala activity led to resolution of the symptoms. As opposed to DBS of the stria terminals, BLn DBS is expected to reduce amygdala.
> 3. The patient did not suffer from a seizure or deterioration in neuropsychological status during chronic DBS for nine months. This suggests an acceptable safety profile of DBS of the amygdala.'
>
> 'Notably, only stimulation of the BLn, but not the central nucleus, the amygdala outflow tract, or neighboring regions affected by other contacts of the stimulating electrodes, led to benefit. Also important was the absence of significant side effects, including seizures.
> While we thus agree that the BLn is not the only potentially valuable target for DBS in PTSD, we believe, based on the rationale described above, that it is the optimal target and it can be modulated safely with current technology.'

Targeting the exact part of the amygdala named Basolateral nucleus (BLn) is more complicated than it is assumed the exact region is defined in [12];

> 'Targeting the BLn is complicated due to anatomical variations in this region. Using a stereotactic atlas, the inferior limit of the BLn is located 16 mm lateral to the AC, 4 mm posterior to the AC and 18 mm inferior to the AC-PC plane.'

Changing in functionality in noradrenergic neurons is believed to be involved in hyperarousal and reexperiencing symptoms of PTSD [2].

PTSD is also defined clearly in [1, p. 2];

> 'PTSD was characterized by three clusters of psychiatric symptoms. The first, re-experiencing, involves the emotional and perceptual reliving of traumatic events either spontaneously or in response to 'triggers' that remind one of the events because they bear some similarity to the original circumstance.'

There are many therapies for PTSD such as Exposure therapy (PE) [3], Cognitive Processing Therapy [4], and Eye Movement Desensitization and reprocessing (EMDR) [5].

The connection between cerebellum and striatum, amygdala and striatum has been explained in [7, p. 489], [9].

> 'Inputs from the cortex primarily project to the striatum.' 'The striatum glutamatergic inputs from several areas, including the cortex, hippocampus, amygdala, and thalamus.'

In [10] they claimed that direct stimulation of the vmPFC can prevent the responsiveness of the amygdala. In [10] it has been claimed that amygdalotomy may regulate and moderate stress level.

3 The Temporal-Causal Network Model

First the Network-Oriented Modelling approach used to model the integrative overall process is briefly explained. As discussed in detail in [16, Chap. 2] this approach is based on temporal-causal network models which can be represented at two levels: by a conceptual representation and by a numerical representation (Fig. 1 and Table 1).

- **Strength of a connection $\boldsymbol{\omega}_{X,Y}$.** Each connection from a state X to a state Y has a *connection weight value* $\boldsymbol{\omega}_{X,Y}$ representing the strength of the connection, often between 0 and 1, but sometimes also below 0 (negative effect) or above 1.
- **Combining multiple impacts on a state $\mathbf{c}_Y$(..).** For each state a *combination function* $\mathbf{c}_Y$(..) is chosen to combine the causal impacts of other states on state Y.
- **Speed of change of a state $\boldsymbol{\eta}_Y$.** For each state Y a *speed factor* $\boldsymbol{\eta}_Y$ is used to represent how fast a state is changing upon causal impact.

Table 1. Explanation of some states and their relation to neurological principles

States	Neurological principles	Quotation, References
ws_c	External stressor	External stress-inducing event [16, 17]
ws_{ee}	World (body) state of extreme emotion *ee*	External stress-inducing event [16]
ss_c	Sensor state for perception of the stressor	'Human states can refer, for example, to states of body parts to see (Eyes), hear (ears) and fee (skin).' In [16, p. 51]
srs_{ee}	Sensory and Feeling representation of stressful event	'The dACC was activated during the observe condition. The dACC is associated with attention and the ability to accurately detect emotional signals.' [2, p. 12] and [13]

(*continued*)

Table 1. (*continued*)

States	Neurological principles	Quotation, References
goal (electrode)	Executive function of stimulation	'Using electrode on basolateral nucleus of Amygdala for Deep brain stimulation'
Hippocampus	Brain parts	Brain parts
Thalamus	Brain parts	Brain parts
Lateral nucleus	component of Amygdala	Lateral part of the Amygdala in brain part
Basolateral nucleus	component of Amygdala (influential for stimulation)	Middle part of the Amygdala in brain part
mPFC	medial Prefrontal Cortex (Reasoning part of brain)	Brain parts
Cerebellum	Brain part	'*The cerebellum receives information from the sensory systems, the spinal cord, and other parts of the brain and then regulates motor movements. The cerebellum coordinates voluntary movements such as posture, balance, coordination, and speech, resulting in smooth and balanced muscular activity*.' [8]
Striatum, mPFC, Hippocampus, Thalamus	Brain part	Brain parts

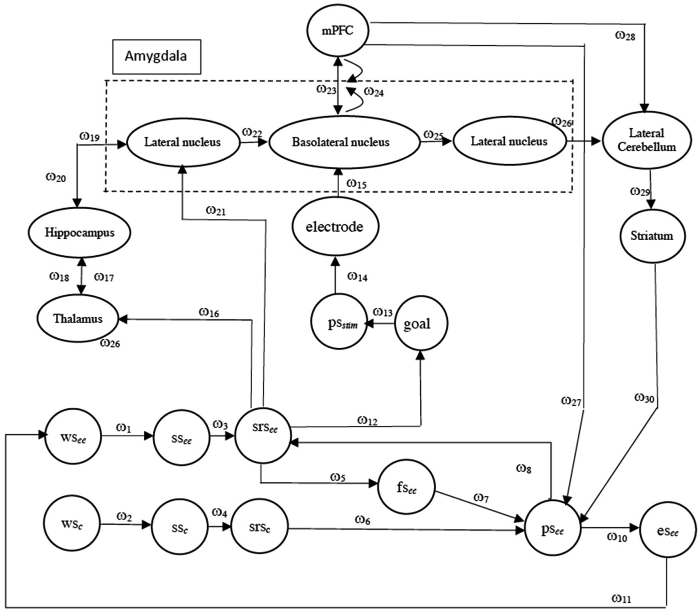

Fig. 1. Conceptual representation of the integrative temporal-causal network model

4 Example Simulation

An example simulation of this process is shown in Fig. 2. Table 2 shows the connection weights used, where the value for ω_{24} is initial value as these weights are adapted over time. The model implemented in the Matlab template provided in [22].

Table 2. Connection weights and scaling factors for the example simulation

Connection weight	ω_1	ω_2	ω_3	ω_4	ω_5	ω_6	ω_7	ω_8	ω_9	ω_{10}	ω_{11}	ω_{12}
Value	1	1	1	1	1	1	1	1	1	1	1	1
Connection weight	ω_{13}	ω_{14}	ω_{15}	ω_{16}	ω_{17}	ω_{18}	ω_{19}	ω_{20}	ω_{21}	ω_{22}	ω_{23}	ω_{24}
Value	1	1	1	1	1	1	1	1	1	1	0.1	0.1
Connection weight	ω_{25}	ω_{26}	ω_{25}	ω_{26}	ω_{27}	ω_{28}	ω_{29}	ω_{30}				
Value	1	1	1	1	−0.9	1	1	−0.5				

Table 3 shows the states which use scale sum function as their combination function. The other states except X_3 (world state of context) and X_{10} (goal) all contains identity function as they have only one incoming connection weight.

Table 3. Scaling factors for the example simulation of states with scale sum function

State	X_5	X_8	X_{13}	X_{14}	X_{15}	X_{16}	X_{17}	X_{19}
λ_i	2	0.8	2	2	2	1	2.1	4

As a biological process, the electrode triggers the activation of Basolateral nucleus in Amygdala at the first state and this impacts other brain parts such as the remarkable one mPFC, left and right lateral nucleus.

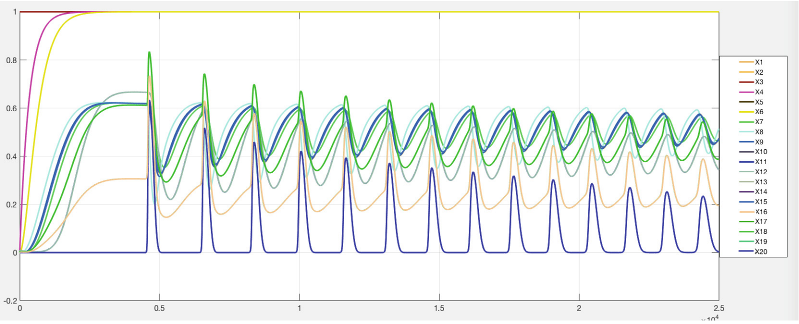

Fig. 2. Simulation results for Deep Brain Stimulation (DBS)

Figure 3 shows a simulation result of using Hebbian learning principle between states basolateral nucleus in amygdala and medial Prefrontal Cortex in one period of using deep brain stimulation.

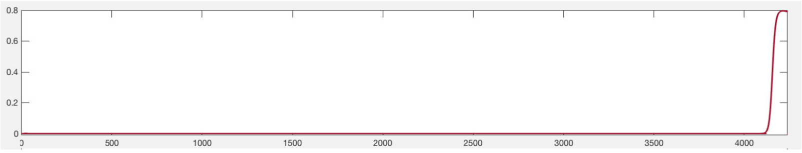

Fig. 3. Simulation results for Deep Brain Stimulation (DBS), Adaptive connections

5 Mathematical Verification

To verify the model that has been proposed mathematical analysis used. For some states in the model the mathematical analysis has been done. Table 4 shows this result. By using the WIMS Linear Solver[1], the following (unique) algebraic solution was obtained for the general case of these equations:

$$X1 = X9$$
$$X2 = X1$$
$$X3 = 1$$
$$X4 = X3$$
$$2 * X5 = 1 * X2 + 1 * X8$$
$$X6 = X4$$
$$X7 = X5$$
$$2 * X8 = 1 * X6 + 1 * X7 - 0.99 * X16 - 0.5 * X20$$
$$X9 = X8$$
$$X10 = 0.2$$
$$X11 = X10$$
$$X12 = X11$$
$$2 * X13 = 1 * X5 + 1 * X14$$
$$2 * X14 = X13 + X15$$
$$X15 = 1 * X14$$
$$X16 = 0.1^{*}X17$$
$$X17 = 0.8 * X14$$
$$X18 = 1 * X17$$
$$2 * X19 = 0.95 * X15$$
$$X20 = X19$$

---

[1] https://wims.unice.fr/wims/wims.cgi?session=K06C12840B.2&+lang=nl&+module=tool%2Flinear%2Flinsolver.en.

Table 4. Scaling factors for the example simulation of states with scale sum function

State	ws_{ee} X_1	ss_{ee} X_2	ws_c X_3	ss_c X_4	srs_{ee} X_5	srs_c X_6	fs_{ee} X_7	ps_{ee} X_8
Simulation	0.7056	0.7047	1,0000	1,0000	0.7029	1,0000	0.6913	0.7209
Analysis	0.7594	0.7594	1,0000	1,0000	0.7594	0.9987	0.7594	0.7594
Deviation	0.0538	0.0547	0,0000	0,0000	0.0565	0.0013	0.0681	0,0385

6 Conclusion

In this paper an integrative cognitive and affective model of therapy by using deep brain stimulation (DBS) for Post-Traumatic Stress Disorder (PTSD) is introduced in which electrode is used. This affects the preparation state of stress and enables to release the stressed person from a chronic stress. This model can be used as the basis of a virtual agent model to get insight in such processes and to bring up a certain cure or treatment of individuals to perform the therapies of extreme emotions for post-traumatic disorder persons.

References

1. Koek, R.J., et al.: Deep brain stimulation of the basolateral amygdala for treatment-refractory combat post-traumatic stress disorder (PTSD): study protocol for a pilot randomized controlled trial with blinded, staggered onset of stimulation. Trials **15**, 356 (2014). https://doi.org/10.1186/1745-6215-15-356
2. Southwick, S.M., et al.: Noradrenergic and serotonergic function in posttraumatic stress disorder. Arch. Gen. Psychiatry **54**, 749–758 (1997)
3. Foe, E., et al.: Randomized trial of prolonged exposure for posttraumatic stress disorder with and without cognitive restricting: outcome at academic and community clinics. J. Consult. Clin. Psychol. **73**, 953–962 (2005)
4. Monson, C.M., Schnurr, P.P., Resick, P.A., Friedman, M.J., Young-Xu, Y., Stevens, S.P.: Cognitive processing therapy for veterans with military-related posttraumatic stress disorder. J. Consult. Clin. Psychol. **74**, 898–907 (2006)
5. Lee, C., Gavriel, H., Drummond, P., Richards, J., Greenwald, R.: Treatment of PTSD: stress inoculation training with prolonged exposure compared to EMDR. J. Clin. Psychol. **58**, 1071–1089 (2002)
6. Andres, M.L., Lipsman, N.: Probing and regulating dysfunctional circuits using deep brain stimulation. Neuron **77**(3), 406–424 (2013). https://doi.org/10.1016/j.neuron.2013.01.020
7. Gazzaniga, S.G., Ivry, R.B., Mangun, G.R.: Cognitive Neuroscience, The Biology of Mind, 2nd edn (2002)
8. https://www.healthline.com/human-body-maps/cerebellum#1
9. Britt, J.P., Benaliouad, F., McDevitt, R.A., Stuber, G.D., Wise, R.A., Bonci, A.: Synaptic and behavioral profile of multiple glutamatergic inputs to the nucleus Accumbens. Neuron **76**, 790–803 (2012). https://doi.org/10.1016/j.neuron.2012.09.040
10. Quirk, G.J., Likhtik, E., Pelletier, J.G., Pare, D.: Stimulation of medial prefrontal cortex decreases the responsiveness of central amygdala output neurons. J. Neurosci. **23**, 8800–8807 (2003)
11. Lee, G.P., et al.: Clinical and physiological effects of stereotaxic bilateral amygdalotomy for intractable aggression. J. Neuropsychiatry Clin. Neurosci. **10**, 413–420 (1998)

12. Langevin, J.P., et al.: Deep brain stimulation of the basolateral amygdala: targeting technique and electrodiagnostic findings. Brain Sci. **6**, 28 (2016)
13. Foote, S.L., Aston-Jones, G., Bloom, E.F.: Impulse activity of locus coeruleus neurons in awake rats and monkeys is a function of sensory stimulation and arousal. Proc. Natl. Acad. Sci. USA **77**, 3033–3037 (1980)
14. Kozarić-Kovačić, D.: Psychopharmacotherapy of posttraumatic stress disorder. Croat. Med. J. **49**(4), 459–475 (2008). https://doi.org/10.3325/cmj.2008.4.459. PMID:18716993
15. Coupland, N.J.: Brain mechanisms and neurotransmitters. In: Post-traumatic Stress Disorder-Diagnosis, Management and Treatment, pp. 69–100. Martin Dunitz, London (2000)
16. Treur, J.: Network-Oriented Modeling: Addressing Complexity of Cognitive, Affective and Social Interactions. Springer, Cham (2016). https://doi.org/10.1007/978-3-319-45213-5
17. Koelsch, S.: Towards a neural basis of music-evoked emotions. Trends Cogn. Sci. **14**, 131–137 (2010). https://doi.org/10.1016/j.tics.2010.01.002
18. Mohammadi Ziabari, S.S., Treur, J.: Cognitive modeling of mindfulness therapy by autogenic training. In: Satapathy, S.C., Bhateja, V., Somanah, R., Yang, X.-S., Senkerik, R. (eds.) Information Systems Design and Intelligent Applications. AISC, vol. 863, pp. 53–66. Springer, Singapore (2019). https://doi.org/10.1007/978-981-13-3338-5_6
19. Mohammadi Ziabari, S.S., Treur, J.: Computational analysis of gender differences in coping with extreme stressful emotions. In: Proceedings of the 9th International Conference on Biologically Inspired Cognitive Architecture (BICA 2018). Elsevier, Amsterdam (2018)
20. Mohammadi Ziabari, S.S., Treur, J.: An adaptive cognitive temporal-causal network model of a mindfulness therapy based on music. In: Tiwary, U.S. (ed.) IHCI 2018. LNCS, vol. 11278, pp. 180–193. Springer, Cham (2018). https://doi.org/10.1007/978-3-030-04021-5_17
21. Treur, J., Mohammadi Ziabari, S.S.: An adaptive temporal-causal network model for decision making under acute stress. In: Nguyen, N.T., Pimenidis, E., Khan, Z., Trawiński, B. (eds.) ICCCI 2018. LNCS (LNAI), vol. 11056, pp. 13–25. Springer, Cham (2018). https://doi.org/10.1007/978-3-319-98446-9_2
22. Mohammadi Ziabari, S.S., Treur, J.: A modeling environment for dynamic and adaptive network models implemented in Matlab. In: Proceedings of the 4th International Congress on Information and Communication Technology (ICICT 2019), 25–26 February 2019. Springer, London (2019)
23. Mohammadi-Ziabari, S.S., Treur, J.: Integrative biological, cognitive and affective modeling of a drug-therapy for a post-traumatic stress disorder. In: Fagan, D., Martín-Vide, C., O'Neill, M., Vega-Rodríguez, M.A. (eds.) TPNC 2018. LNCS, vol. 11324, pp. 292–304. Springer, Cham (2018). https://doi.org/10.1007/978-3-030-04070-3_23
24. Lelieveld, I., Storre, G., Mohammadi Ziabari, S.S.: A temporal cognitive model of the influence of methylphenidate (Ritalin) on test anxiety. In: Proceedings of the 4th International Congress on Information and Communication Technology (ICICT 2019), 25–26 February 2019. Springer, London (2019)
25. Andrianov, A., Guerriero, E., Mohammadi Ziabari, S.S.: Cognitive modeling of mindfulness therapy: effects of yoga on overcoming stress. In: Proceedings of the 16th International Conference on Distributed Computing and Artificial Intelligence (DCAI 2019), 26-28 June. Avila, Spain (2019)
26. E de Haan, R., Blanker, M., Mohammadi Ziabari, S.S.: Integrative biological, cognitive and affective modeling of caffeine use on stress. In: Proceedings of the 16th International conference on Distributed Computing and Artificial Intelligence (DCAI 2019), 26-28 June. Avila, Spain (2019)
27. Mohammadi Ziabari, S.S.: An adaptive temporal-causal network model for stress extinction using fluoxetine. In: Proceedings of the 15th International Conference on Artificial Intelligence Applications and Innovations (AIAI 2019), 24–26 May 2019, Crete, Greece (2019)