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Research article

An adaptive Network-Oriented cognitive model for Major Depression and its treatment

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ABSTRACT

This paper presents an adaptive neurologically inspired cognitive model for Major Depressive Disorder. It is based on an (adaptive) temporal-causal network modelling approach incorporating a dynamic perspective on mental states and causal relations. The adaptive network model addresses how a Deep Brain Stimulation treatment used for this disorder can work by a Hebbian learning effect.

Introduction

Individuals can be in a depressed mood due to stressful experiences, loss of a loved one or feeling guilty about something. This does not necessarily mean that they are diagnosed with Major Depressive Disorder (MDD). Major Depression is a common and also costly disorder associated with severe and persistent symptoms, causing social impairment, increased medical co-morbidity and mortality [7]. Over the years, the development of animal models and genetics progressed in order to investigate the etiology of Major Depressive Disorder; e.g., (Abelaira, Reus, & Quevedo, 2013; Kudryavtseva, Bakshtnovskaya, & Koryakina, 1991; Nestler et al., 2002; Nestler & Hyman, 2010; Smoller, 2016). Although these models can provide understanding of behavioural aspects, there are limitations. Symptoms used to establish the disorder in humans, for example, hallucinations, guilt, sadness, cannot be convincingly ascertained in animals. Knowledge about what the exact pattern of structural brain alterations are when suffering Major Depression Disorder (Schmaal, Veltman, & van Erp, 2016) is available but still limited. It is important to get a better insight in mechanisms that enable treatments to have their effect. Computational cognitive modelling can contribute to this.

To develop a computational cognitive model it is important to consider the network of mental states that play a role and in particular also to address the dynamics and interaction within this network. These dynamics also concern adaptivity, as network connections between mental states usually change over time by learning. The Network-Oriented Modelling approach described in (Treur, 2016a, 2016b, 2018) enables to cover this. The basic (nonadaptive) cognitive model presented as a first step addresses three different types of subjects and their behaviour: a healthy person where the mental processes do not have alterations and the behaviour is normal, someone feeling depressed and expressing it even though there are no real deficits, and a person suffering Major Depression Disorder. The adaptive cognitive model presented next shows how adaptivity of the strength of connections between mental states by Hebbian learning (Hebb, 1949) plays a role and can be affected by treatment, illustrated for a Deep Brain Stimulation treatment. Such a treatment makes that some specific parts of the brain get enhanced activation levels. By Hebbian learning such enhanced activations can lead to better learning.

This paper focuses on the type without mania (Carlson, 2014; Demic & Cheng, 2014): Major Depression Disorder (MDD). Evidence indicates (Schmaal et al., 2016) that a tendency of developing MDD is a heritable characteristic; several genes have been found that relate to MDD. At the level of the brain also alterations and deficits in pathways have been found (Carlson, 2014). A number of brain areas and connections are known to influence the onset of MDD (Belden et al., 2016; Carlson, 2014). Brain imaging studies have presented that deficits in reward processing contribute to Major Depressive Disorder. Especially, the dorsal lateral prefrontal cortex (DLPFC), Nucleus Accumbens and the Amygdala play a part in this reward circuitry and emotion regulation (Belden et al., 2016). The DLPFC is connected with the Amygdala and plays an important role in inhibition of it, controlling expression of negative emotional responses. However, people suffering Major Depression Disorder show a decreased activity of the DLPFC and therefore less inhibition of the Amygdala, which leads to increased activity of the Amygdala. Due to this impaired interaction, the inhibition is low resulting in irregularity of the circuits and behaviour (Carlson, 2014; Greg, Thompson, Carter, Steinhauer, & Thase, 2007). The computational cognitive models introduced in this paper take the bidirectional connections between the DLPFC and Amygdala into account, as discussed above. The basic model shows the differences of the dynamic mental processes occurring in healthy persons, persons feeling depressed and persons suffering Major Depressive Disorder. The adaptive computational cognitive model shows how stronger or weaker

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connections from Amygdala to DLPFC can evolve over time and affect the MDD, and how a Deep Brain Stimulation treatment can strengthen them.

In this paper, the basic cognitive model is presented in Section "The basic cognitive model for MDD". Section "Simulation experiments for the basic cognitive model" discusses some of the simulation results of the model. In Section "An adaptive cognitive model for MDD and DBS-treatment", the adaptive cognitive model is introduced and the influence of a Deep Brain Stimulation treatment used by people suffering Major Depression Disorder is shown. Simulation results of this are shown in Section "Simulation experiments for the adaptive cognitive model". In Section "Verification" verification is addressed. Finally, Section "Discussion" is a discussion.

The basic cognitive model for MDD

The basic and adaptive cognitive models have been designed using the Network-Oriented Modelling approach described in (Treur, 2016a, 2016b); see also (Treur, 2018). The network can be designed at a conceptual level (Treur, 2016b). A (graphical) conceptual representation displays in a graphical manner nodes for *states* and arrows for *connections* indicating causal impacts from one state to another. The model was designed by considering a few aspects of Major Depression, based on the literature with focus on Prefrontal Cortex bi-directionally connected with Amygdala, and preparations for actions to express a particular (negative) feeling induced by a stimulus s (a negative event). In Fig. 1 a graphical conceptual representation of the basic cognitive model is depicted and in Table 1 the concepts used are explained. Sensory representation states srs_s, srs_{int} are used as internal representations for stimulus s and the body state that embodies the emotional response state.

For stimulus s the sensor state ss_s is used to incorporate the sensing from world state ws_s of s. The sensory representation of a stimulus has an impact on the preparation state ps_{int} for a bodily response. By a predictive as-if body loop this leads to sensory internal body representation state srs_{int}, and subsequently this has impact on the preparation state ps_{int}, which makes the process a recursive as-if body loop (Treur, 2016b).

The execution state es_{int} is included for expression of the prepared body state. Both the preparation state and the actual execution are affected by the control state $cs_{s,int}$ representing the role of the prefrontal cortex. The following elements are the main elements of a conceptual representation:

- For each connection from state X to state Y a *weight* $\boldsymbol{\omega}_{X,Y}$ (a number between -1 and 1), for strength of impact (a negative weight is used for suppression)
- For each state Y a *speed factor* $\boldsymbol{\eta}_Y$ (a positive value) for timing of impact
- For each state Y a *combination function* $\mathbf{c}_Y(\ldots)$ used to aggregate multiple impacts from different states on one state Y; see below for some examples

Table 1
Overview of the states used in the basic cognitive model.

State	Explanation
ws_s	The current world state: the person is facing stimulus s (a negative event)
ss_s	Sensory state which the person senses the world through
srs_s	Sensory representation state of stimulus s
srs_{int}	Sensory representation state of internal body state of the amygdala
ps_{int}	Preparation state for internal body state, characterizing the amygdala responses
$cs_{s,int}$	Control state for stimulus s, characterizing the prefrontal cortex
es_{int}	Execution state for the internal body state

For a numerical representation of the model the states Y get activation values indicated by $Y(t)$: real numbers between 0 and 1 over time points t, where the time variable t ranges over the real numbers.

A conceptual representation of as shown in Fig. 1 can be transformed in a systematic or even automated manner into a numerical representation as follows [20]:

- At each time point t state X connected to state Y has an impact on Y defined as $\mathbf{impact}_{X,Y}(t) = \omega_{X,Y}X(t)$. where X, Y . is the weight of the connection from X to Y
- The *aggregated impact* of multiple states X_i on Y at t is determined using a *combination function* $\mathbf{c}_Y(\ldots)$:

$$\mathbf{aggimpact}_Y(t) = \mathbf{c}_Y\left(\mathbf{impact}_{X_1,Y}(t), \ldots, \mathbf{impact}_{X_k,Y}(t)\right) = \mathbf{c}_Y\left(\omega_{X_1,Y}X_1(t), \ldots, \omega_{X_k,Y}X_k(t)\right)$$

where X_i are the states with outgoing connections to state Y

- The effect of $\mathbf{aggimpact}_Y(t)$. on Y is exerted over time gradually, depending on *speed factor* η_Y:

$$Y(t + \Delta t) = Y(t) + \eta_Y[\mathbf{aggimpact}_Y(t) - Y(t)]\Delta t$$

$$\frac{dY(t)}{dt} = \eta_Y[\mathbf{aggimpact}_Y(t) - Y(t)]$$

Thus the following *difference* and *differential equation* for Y are obtained:

$$Y(t + \Delta t) = Y(t) + \eta_Y\left[\mathbf{c}_Y\left(\omega_{X_1,Y}X_1(t), \ldots, \omega_{X_k,Y}X_k(t)\right) - Y(t)\right]\Delta t$$

$$\frac{dY(t)}{dt} = \eta_Y\left[\mathbf{c}_Y\left(\omega_{X_1,Y}X_1(t), \ldots, \omega_{X_k,Y}X_k(t)\right) - Y(t)\right]$$

As an example, according to the numerical representation described above, the difference and differential equation for the control state $cs_{s,int}$ are as follows:

$$cs_{s,int}(t + \Delta t) = cs_{s,int}(t) +$$

$$\eta_{cs_{s,int}}\left[\mathbf{c}_{cs_{s,int}}\left(\omega_{srs_s,cs_{s,int}}srs_s(t), \omega_{ps_{int},cs_{s,int}}ps_{int}(t)\right) - cs_{s,int}(t)\right]\Delta t$$

$$\frac{dcs_{s,int}(t)}{dt} =$$

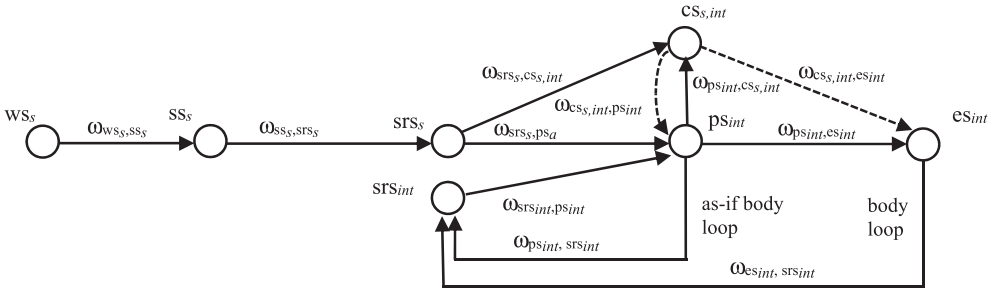

Fig. 1. Conceptual representation of the basic cognitive model for MDD.

$$\eta_{cs_{s,int}}\left[\mathbf{c}_{cs_{s,int}}\left(\omega_{srs_s,\,cs_{s,int}}srs_s(t),\,\omega_{ps_{int},\,cs_{s,int}}ps_{int}(t)\right)-cs_{s,int}(t)\right]$$

So, for every set of instances or values for the connection weights, speed factors and combination functions, a difference or differential equation is assigned to each state of the model. In the model considered here, it makes a set of 6 coupled difference or differential equations, that together describe the behaviour of the model when in mutual interaction. For all states either the *identity function* **id(…)** or the *advanced logistic sum combination function* $\mathbf{alogistic}_{\sigma,\tau}(\ldots)$ is used as combination function [20]:

$$\mathbf{c}_Y(V)=\mathbf{id}(V)=V$$

$$\mathbf{c}_Y(V_1,\ldots,V_k)=\mathbf{alogistic}_{\sigma,\tau}(V_1,\ldots,V_k)=\left(\frac{1}{1+e^{-\sigma(V_1+\ldots+V_k-\tau)}}-\frac{1}{1+e^{\sigma\tau}}\right)(1+e^{-\sigma\tau})$$

Here σ is a *steepness* parameter and τ a *threshold* parameter. The advanced logistic sum combination function has the property that activation levels 0 are mapped to 0 and it keeps values below 1. The function $\mathbf{alogistic}_{\sigma,\tau}(\ldots)$ is used for 4 states with multiple impacts: cs_s, ps_{int}, srs_{int}, es_{int}. For example, for the control state $cs_{s,int}$, the model is numerically represented in difference and differential equation form as:

$$cs_{s,int}(t+\Delta t)=cs_{s,int}(t)+$$

$$\eta_{cs_{s,int}}\left[\mathbf{alogistic}_{\sigma,\tau}\left(\omega_{srs_s,\,cs_{s,int}}srs_s(t),\,\omega_{ps_{int},cs_{s,int}}ps_{int}(t)\right)-cs_{s,int}(t)\right]\Delta t$$

$$\frac{dcs_{s,int}(t)}{dt}=\eta_{cs_{s,int}}\left[\mathbf{alogistic}_{\sigma,\tau}\left(\omega_{srs_s,\,cs_{s,int}}srs_s(t),\,\omega_{ps_{int},\,cs_{s,int}}ps_{int}(t)\right)-cs_{s,int}(t)\right]$$

Simulation experiments for the basic cognitive model

The basic cognitive model described in Section "The basic cognitive model for MDD" has been used to conduct a number of simulation experiments to show three different types of person; healthy, feeling depressed and suffering Major Depression. In order to show the processes and behaviour in a realistic manner, according to the neurobiological background in Section "The basic cognitive model for MDD", the parameters for the connection weights will be different for a person with MDD, especially those connecting the PFC with the Amygdala. In the example discussed here these parameters have been chosen as shown in Table 2. People who are healthy do not have any impairments of connections between different brain area's (e.g., relatively high strengths for $\omega_{srs_s,cs_{s,int}}$ and $\omega_{ps_{int},cs_{s,int}}$ enabling a form of monitoring of the emotional state). It is the same for people just feeling depressed; although those people do not have any impairments like for Major Depression, there are connections with lower impact due to a bad feeling state they have. People suffering MDD have impairments of connections; e.g., low $\omega_{srs_s,cs_{s,int}}$ and $\omega_{ps_{int},cs_{s,int}}$ resulting in less inhibition of the Amygdala, even when the suppression connection from PFC to Amygdala has a higher negative $\omega_{cs_{s,int},ps_{int}}$. It has been found that higher negative feeling levels usually co-occur with lower levels of PFC activity; e.g., see (Treur, 2016b), p. 153 and the literature referred there. To model this, for the MDD case the upward connection weight $\omega_{ps_{int},cs_{s,int}}$ has been set at a low value, so that the PFC state is not activated much by the negative feeling. Note that personal characteristics as represented by the parameters used here always vary over persons. This also applies to groups diagnosed for a certain disorder.

For the simulations the step size Δt was 0.5, all speed factors were 0.5, and all other connection weights were 1. Furthermore, for the states that use the advanced logic combination function, the steepness σ and threshold τ values used are as in Table 3.

Table 3
Steepness σ and threshold τ parameter values used in the model.

Person	State	σ	τ
Healthy	$cs_{s,int}$, srs_{int}, ps_{int}, es_{int}	30	0.3
Feeling Depressed	$cs_{s,int}$, srs_{int}, ps_{int}, es_{int}	30	0.3
Major Depression	$cs_{s,int}$, srs_{int}, ps_{int}, es_{int}	40	0.4

The initial values of activation levels for all states have been chosen 0, except the world state ws_s which had a constant value of 1 as a form of input (a stressful circumstance) for the model. Fig. 2 shows the simulation results of a healthy person (e.g., $\omega_{srs_s,cs_{s,int}}=0.7$, $\omega_{cs_{s,int},ps_{int}}=-0.3$, $\omega_{ps_{int},cs_{s,int}}=0.6$; see Table 2, last row).

The control state becomes active to cope with the stressful stimulus. In the first few steps, all values go up. Fig. 2 also shows that the sensory representation state value of the internal process (srs_{int}, Amygdala circuit) stays lower, as the activity of that area is less than others (Carlson, 2014). Fig. 3 shows the simulation of a person feeling depressed (see Table 2, middle row). Again the control state becomes active. However, there is slightly more activity of the srs_{int} (Amygdala circuit) making someone react stronger towards negative stimulus and expressing similar symptoms of MDD. Fig. 4 shows the simulation of a person suffering Major Depression Disorder (see Table 2, second row). In this case there is lower activity of the control state. In the first few steps all values go up. Time point 10 shows a fast decline of the expressive behaviour due to the strong suppressive effect of $\omega_{cs_{s,int},ps_{int}}$. Because in the simulation the stressful stimulus never fades away, the depression stays too. The symptoms described in Section "Introduction" will be expressed by the person.

An adaptive cognitive model for MDD and DBS-treatment

In order to alleviate symptoms of MDD, most of the time doctors prescribe antidepressants like selective serotonin reuptake inhibitors (SSRI's) (El Mansari et al., 2010; Nemeroff, 2002; Shirayama, Chen, Nakagawa, Russell, & Duman, 2002). Even though these treatments have proved to be successful, not every patient responds to it. Therefore, a new treatment has been developed recently, called Deep Brain Stimulation (DBS). In this treatment electrodes are placed at specific brain area's in order to stimulate the pathways between them (Schlaepfer et al, 2008; Schlaepfer, Bewernick, Kayser, Hurlemann, & Coenen, 2014). A principle that explains the effect of this treatment is Hebbian learning (Hebb, 1949): when two connected neurons are activated simultaneously, their connection will strengthen. So, when these connected neurons are activated in an artificial manner by DBS it may be expected that this DBS treatment will make their connection stronger. An adaptive temporal-causal network modelling based on Hebbian Learning was designed to cover this. The DBS-supported Hebbian learning approach is applied to the upward connection from Amygdala to PFC in the core part of the basic cognitive model, as it has been found that lower PFC activity correlates to higher levels of negative feelings (see (Treur, 2016b), p. 153); see Fig. 5. Actually this upward arrow stands for a pathway, parts of which are stimulated by DBS. In Fig. 5 the solid curvy arrows indicate how the connection weight $\omega_{ps_{int},cs_{s,int}}$ is affected by activation of the states ps_{int} and $cs_{s,int}$

Table 2
Values of parameters used as connection weight.

Weight	$\omega_{srs_s,cs_{s,int}}$	$\omega_{cs_{s,int},ps_{int}}$	$\omega_{ps_{int},cs_{s,int}}$	$\omega_{srs_{int},cs_{s,int}}$	$\omega_{cs_{s,int},es_{int}}$	$\omega_{srs_s,ps_{int}}$	$\omega_{srs_{int},ps_{int}}$	$\omega_{ps_{int},srs_{int}}$	$\omega_{es_{int},srs_{int}}$	$\omega_{ps_{int},es_{int}}$
MDD	0.2	−0.8	0.2	0.1	-0.6	0.9	0.8	0.6	0.4	0.6
Depressed	0.7	−0.3	0.6	0.8	-0.2	0.9	0.8	0.2	0.3	0.5
Healthy	0.7	−0.3	0.6	0.8	-0.2	0.7	0.4	0.1	0.2	0.7

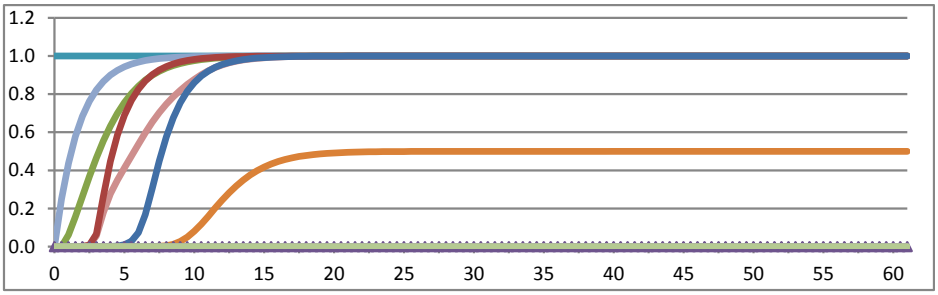

Fig. 2. Simulation of a Healthy Person. Horizontal axis: time. Vertical axis: activation value. Orange: $cs_{s.int}$ (prefrontal cortex activity). Green: srs_{int} (Amygdala circuitry) Dark blue: es_{int} (expressing normal behaviour).

due to Hebbian learning (for more details of Hebbian learning in temporal-causal networks, see (Treur, 2016b), Ch 2, Section 2.10). Moreover, ts_{DBS} is the treatment state of the device inducing the DBS stimulation and the dotted arrows indicate the effect of this device on some of the brain states.

Note that because the connection weight is now considered a variable, it can be modelled as a state in the network as well; for more details, see also (Treur, 2016b), pp. 92–98. Numerically, the connection weight $\omega_{ps_{int},cs_{s,int}}$ is adapted using the following specific Hebbian learning rule (also see [20]), taking a maximal connection weight of 1 into account, a *learning rate* $\eta > 0$, and a *persistence factor* μ in the interval [0, 1], and the activation levels $ps_{int}(t)$ and $cs_{s,int}(t)$. The persistence factor μ determines how much extinction takes place. When it is 1 no extinction takes place, and the lower it is, the more extinction takes place. The format is based on the combination function $\mathbf{c}(\ldots)$ defined by

$$\mathbf{c}(X,\ Y,\ W) = X\ Y\ (1-W) + \mu\ W$$

and filled with the states $ps_{int}(t)$, $cs_{s,int}(t)$, $\omega_{ps_{int},cs_{c,int}}(t)$ for X, Y, W considered here:

$$\mathbf{c}(ps_{int}(t), cs_{s,int}(t), \omega_{ps_{int}, cs_{s,int}}(t)) = ps_{int}(t)cs_{s,int}(t)\left(1-\omega_{ps_{int}, cs_{s,int}}(t)\right) + \mu\omega_{ps_{int}, cs_{s,int}}(t)$$

$$\frac{d\omega_{ps_{int}, cs_{s,int}}(t)}{dt} = \eta\left[ps_{int}(t)cs_{s,int}(t)\left(1-\omega_{ps_{int}, cs_{s,int}}(t)\right) + \mu\omega_{ps_{int}, cs_{s,int}}(t) - \omega_{ps_{int}, cs_{s,int}}(t)\right]$$

$$\omega_{ps_{int}, cs_{s,int}}(t+\Delta t) = \omega_{ps_{int}, cs_{s,int}}(t) + \eta\left[ps_{int}(t)cs_{s,int}(t)\left(1-\omega_{ps_{int}, cs_{s,int}}(t)\right) + \mu_{ps_{int}, cs_{s,int}}(t) - \omega_{ps_{int}, cs_{s,int}}(t)\right]\Delta t$$

Simulation experiments for the adaptive cognitive model

The following Fig. 6 shows the learning of this weight $\omega_{ps_{int},cs_{s,int}}$ using Hebbian learning, for different scenarios including one with a treatment based on Deep Brain Stimulation. Fig. 6(a) (two upper graphs) shows the response and connection weight for a healthy person. The persistence parameter μ is 1 here. The top figure illustrates the activity of the PFC (brown line) and Amygdala (pink line) during the normal condition described in the previous section. The green line represents the internal connection between the two brain areas. As can be seen in the lower graph in the figure, the connection weight is raising towards one. This means for this person the brain areas and reactions are behaving according to normal standards.

The graphs in Fig. 6(b) illustrate the activity and learning effect of person with MDD. The persistence parameter μ is 0.5 in this case. As can be seen the Pre-Frontal Cortex does not have any or almost no

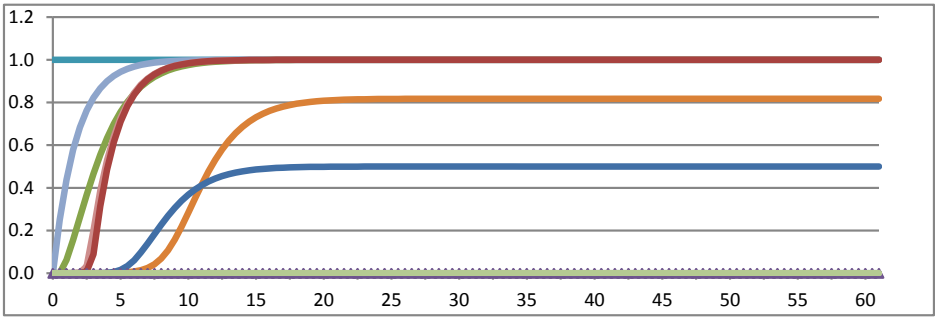

Fig. 3. Simulation of a Person feeling depressed. Orange: $cs_{s,int}$ (prefrontal cortex activity). Green: srs_{int} (amygdala circuitry) Dark blue: es_{int} (expressing behaviour).

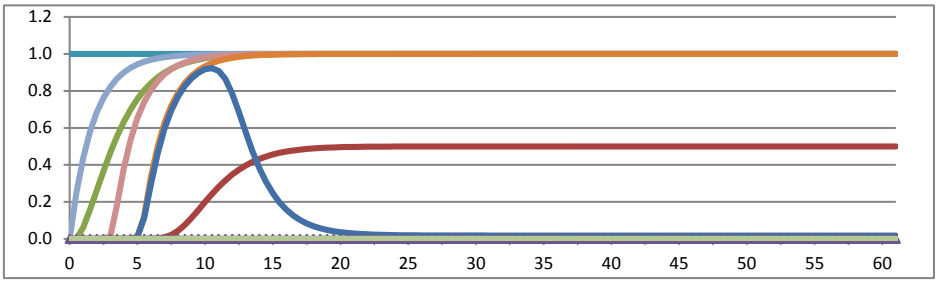

Fig. 4. Simulation of a Person with Major Depression. Orange: $cs_{s,int}$ (prefrontal cortex activity). Green: srs_{int} (amygdala circuitry) Dark blue: es_{int} (expressing).

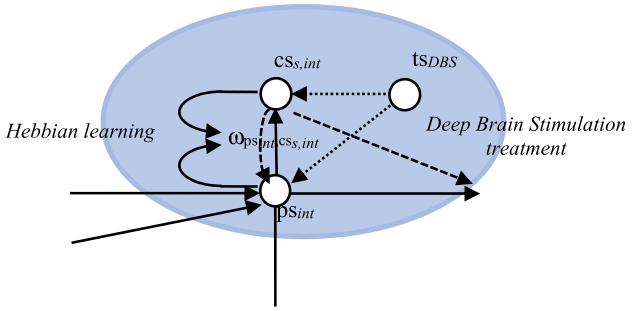

Fig. 5. Conceptual representation of part of the adaptive cognitive model incorporating Hebbian learning (the curvy arrows) and Deep Brain Stimulation (DBS) treatment (by the state ts_{DBS} and its connections indicated by dotted arrows).

activity while the Amygdala is hyperactive [6].

There is no treatment applied in this case and therefore the connection weight $\omega_{ps_{int},cs_{s,int}}$ is decreasing to zero due to extinction, as not enough learning takes place to compensate for extinction. So, Fig. 6(a) and (b) imply that there is a significant difference in activity and learning effect between a healthy person and someone suffering from Major Depression Disorder. Fig. 6(c) shows simulation results for the adaptive network for a person with MDD undergoing a Deep Brain Stimulation treatment. The persistence parameter **μ** is 0.5. The activities of the different brain areas, illustrated in the top figure, display improvement regarding unhealthy people but not yet to normal standards (Carlson, 2014). The learning effect for the treatment is shown in the bottom figure, there is an increase of this rate indicating some persons, as described in Section "Introduction", are improving and therefore feeling less depressing and relieving symptoms. It is not the same as a healthy person but it shows the persistent factor of treatment is helpful for patients suffering Major Depression Disorder.

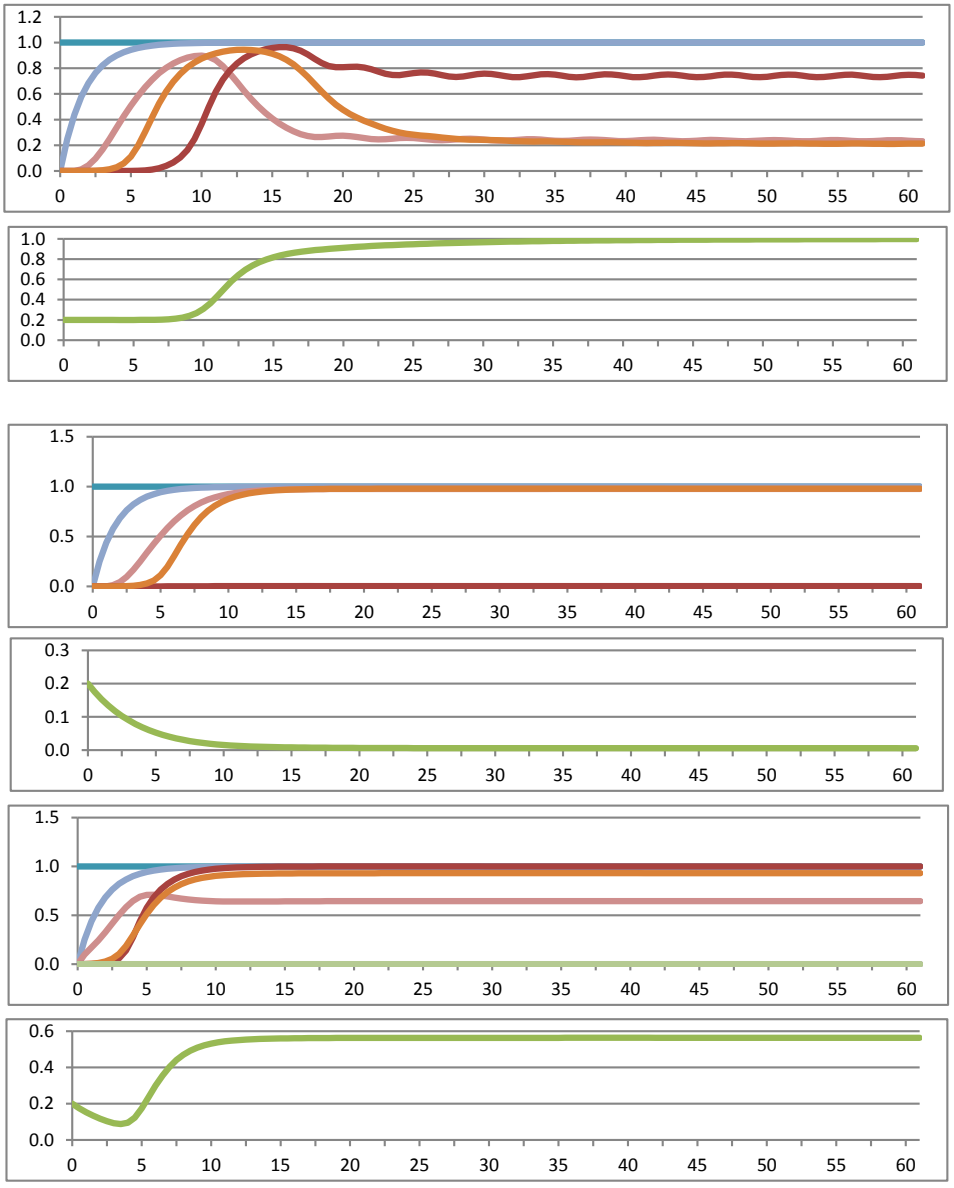

Fig. 6. Adaptive Simulations (a) a Healthy Person. Topmost graph: Brown cs_s (prefrontal cortex activity). Pink: srs_{int} (amygdala circuitry) Green: srs_s (internal connection). Second graph: effect of the learning on the connection weight $\omega_{ps_{int},cs_{s,int}}$. (b) a Person suffering from MDD without treatment. Third graph: Brown: cs_s (prefrontal cortex activity). Pink: srs_{int} (amygdala circuitry) Green: srs_s (internal connection). Fourth graph: effect of the lack of learning on the connection weight $\omega_{ps_{int},cs_{s,int}}$. (c) a Person suffering from MDD with Deep Brain Stimulation treatment. Fifth graph: Brown: cs_s (prefrontal cortex activity). Pink: srs_{int} (amygdala circuitry) Green: srs_s (internal connection). Bottom graph: effect of the DBS-supported Hebbian learning on the connection weight $\omega_{ps_{int},cs_{s,int}}$.

Table 4
Verification results.

Type	μ	Time	$ps_{int}(t)$	$cs_{s,int}(t)$	$\omega_{ps_{int},cs_{s,int}}(t)$	$\frac{ps_{int}(t)\ cs_{s,int}(t)}{(1-\mu)+ps_{int}(t)\ cs_{s,int}(t)}$	Deviation
Healthy	1	60	0.23592	0.74940	0.99781	1.00000	−0.00218
Unhealthy	0.5	60	0.97702	0.00291	0.00567	0.00567	$2.4724 \cdot 10^{-7}$
Unhealthy with DBS	0.5	60	0.64559	0.999999	0.56354	0.56355	$-7.0461 \cdot 10^{-10}$
Healthy	1	300	0.23349	0.73873	1.00000	1.00000	$-1.2123 \cdot 10^{-12}$
Unhealthy	0.5	300	0.97703	0.00292	0.00567	0.00567	0
Unhealthy with DBS	0.5	300	0.64559	0.999999	0.56355	0.56355	0

Verification

Usually dynamic properties of dynamic cognitive models can be analysed by conducting simulation experiments. But sometimes, as a kind of prediction properties can also be found by calculations in a mathematical manner, without performing simulations. Such types of properties found in an analytic mathematical manner can be used for verification of the model by checking them for the values observed in simulation experiments. This particular use of mathematical analysis as discussed here focuses on stationary points: state Y has a *stationary point* at t if $\mathbf{d}Y(t)/\mathbf{d}t = 0$. In the graphs shown in the Fig. 6 it seems that equilibria are reached. The question then is whether these observations based on simulation experiments are in agreement with a mathematical analysis based on the formal model specifications. If it is found out that they are in agreement with the mathematical analysis, then this provides some extent of evidence that the implemented model is correct. If they turn out not to be in agreement with the mathematical analysis, then further inspection and correction has to be initiated. Within the numerical representation of temporal-causal networks the differential equations have a specific format, and then the following criterion applies:

Y has a stationary point at $t \Leftrightarrow \mathbf{c}_Y(\omega_{X_1,Y}\ X_1(t),\ \ldots,\ \omega_{X_k,Y}\ X_k(t)) = Y(t)$

with $X_1, \ldots, X_k$ the states with outgoing connections to Y

Consider the adaptive connection from ps_{int} to $cs_{s,int}$; the criterion for stationary point is:

$$\mathbf{c}\left(ps_{int}(t),\ cs_{s,int}(t),\ \omega_{ps_{int},cs_{s,int}}(t)\right) = \omega_{ps_{int},cs_{s,int}}(t)$$

$$ps_{int}(t)cs_{s,int}(t)\left(1-\omega_{ps_{int},cs_{s,int}}(t)\right) + \mu\omega_{ps_{int},cs_{s,int}}(t) = \omega_{ps_{int},cs_{s,int}}(t)$$

Simplifying the notation by putting $X = ps_{int}$, $Y = cs_{s,int}$, $\omega = \omega_{ps_{int},cs_{s,int}}$ and leave out the time from the notation provides the following criteria for ω:

ω stationary ⇔

$$X\ Y\ (1-\omega) + \mu\omega = \omega \Leftrightarrow$$

$$\omega = \frac{X\ Y}{(1-\mu)+X\ Y}$$

The above criterion has been applied to verify whether the adaptive cognitive model is correct with respect to its formal mathematical specifications; see Table 4. In particular, the final stationary points have been inspected for the three scenarios shown in Fig. 6. As seems in these figures, in all three cases the model is heading to a joint stationary point for all states and connections (also called an equilibrium state). In the first three rows of Table 4 it is shown which values are reached at time 60 (the last time point shown in the Fig. 6) for $cs_{s,int}(t)$, $\omega_{ps_{int},cs_{s,int}}(t)$ and $\omega_{ps_{int},cs_{s,int}}(t)$. In the seventh column the criterion for $\omega_{ps_{int},cs_{s,int}}(t)$ is calculated and in column 8 the deviation of the criterion from the actual value of $\omega_{ps_{int},cs_{s,int}}(t)$ is determined. As can be seen in this last column, the deviations are less than 10^{-2}. To see how the situation is after a longer time period, the simulations also have been done up till time point 300. The results for this are shown in the last three rows of Table 4. As can be seen, now the deviations are less than 10^{-11}. These results give evidence that the model does what is expected.

Discussion

The cognitive model presented in this paper provide neurologically inspired computational models for the field of Major Depression, enabling to distinguish the differences in mental processes of different types of subjects. The models were designed as networks of mental states according to the temporal-causal network modelling approach described in (Treur, 2016a, 2016b, 2018). Within the presented adaptive cognitive model Hebbian learning (Hebb, 1949) has been incorporated. Using proper values of parameters, such as connection weights, the models can simulate the differences between a healthy person, a person feeling depressed and a person suffering Major Depression. Persons whom were diagnosed with MDD and do not get treatment were compared with the ones who do get treatment by Deep Brain Stimulation; this comparison shows a significant difference in behaviour and functioning of brain areas. Verification has been performed to test whether the simulations are in accordance with what can be predicted from the formal model specifications by mathematical analysis.

The cognitive model presented here can be used to develop human-aware intelligent systems (Azziz, Klein, & Treur, 2010; Bosse, Callaghan, & Lukowicz, 2010) that can provide help getting more understanding of the deficits and impaired pathways, supporting persons suffering from Major Depression Disorder. Treatments, especially Deep Brain Stimulation, have proven to be effective (El Mansari et al., 2010; Schlaepfer et al, 2008; Schlaepfer et al., 2014) and a computational model can be of benefit to the research for treatments and biology of MDD. In future work, the models may be extended with more characteristics as the research in the field of Major Depression Disorder is progressing. In addition, a focus can be set also on environmental and social factors. Comparison with numerical empirical data would be interesting, but such data were not available. Nevertheless, for now in empirical literature qualitative empirical indications were found and the model was able to generate behaviour that is in accordance with them.

References

Abelaira, H. M., Reus, G. Z., & Quevedo, J. (2013). Animal models as tools to study the pathophysiology of depression. *Revista Brasileira Psiquiatria, 35*, 112–120.
Azziz, A. A., Klein, M. C. A., & Treur, J. (2010). An integrative ambient agent model for unipolar depression relapse prevention. *Journal of Ambient Intelligence and Smart Environments, 2*, 5–20.
Belden, A. C., Irvin, K., Hajcak, G., Kappenman, E. S., Kelly, D., Karlow, S., et al. (2016). Neural correlates of reward processing in depressed and healthy preschool-age children. *Journal of the American Academy of Child & Adolescent Psychiatry, 55*(12), 1081–1089.
Bosse, T., Callaghan, V., & Lukowicz, P. (2010). On computational modeling of human oriented knowledge in Ambient Intelligence. *Journal of Ambient Intelligence and Smart Environments, 2*, 3–4.
Hebb, D. O. (1949). *The organisation of behaviour.* Wiley Publishers.
Carlson, N. R. (2014). *Foundations of behavioral neuroscience* (9th ed.). Harlow: Pearson483–492.
Demic, S., & Cheng, S. (2014). Modeling the dynamics of disease states in depression.

PLoS One, 9(10), e110358.
Greg, J. S., Thompson, W., Carter, C. S., Steinhauer, S. R., & Thase, M. E. (2007). Increased amygdala and decreased dorsolateral prefrontal BOLD responses in unipolar depression: Related and independent features. *Biological Psychiatry, 62*(2), 198–209.
Kudryavtseva, N. N., Bakshtnovskaya, I. V., & Koryakina, L. (1991). A social model of depression in mice of c57BL/6J strain. *Pharmacology Biochemistry & Behavior, 38*, 315–320.
El Mansari, M., et al. (2010). Relevance of norepinephrine–dopamine interactions in the treatment of major depressive disorder. *CNS Neuroscience & Therapeutics, 16*(3), e1–e17.
Nemeroff, C. B., et al. (2002). Duloxetine for the treatment of major depressive disorder. *Psychopharmacology Bulletin, 36*(4), 106–132.
Nestler, E. J., Barrot, M., DiLeone, R. J., Eisch, A. J., Gold, S. J., & Monteggia, L. M. (2002). Neurobiology of depression. *Neuron, 34*, 13–25.
Nestler, E. J., & Hyman, S. E. (2010). Animal models of neuropsychiatric disorders. *Nature Neuroscience, 13*(10), 1161–1169.
Schlaepfer, T. E., Bewernick, B. H., Kayser, S., Hurlemann, R., & Coenen, V. A. (2014). Deep brain stimulation of the human reward system for major depression: Rationale, outcomes and outlook. *Neuropsychopharmacology, 39*, 1303–1314.
Schlaepfer, T. E., Cohen, M. X., Frick, C., Kosel, M., Brodesser, D., Axmacher, N., et al. (2008). Deep brain stimulation to reward circuitry alleviates anhedonia in refractory major depression. *Neuropsychopharmacology, 33*(2), 368–377.
Schmaal, L., Veltman, D. J., van Erp, T. G. M., et al. (2016). Subcortical brain alterations in major depressive disorder: Findings from the EIGMA Major Depressive Disorder working group. *Molecular Psychiatry, 21*, 806–812.
Shirayama, Y., Chen, A. C. H., Nakagawa, S., Russell, D. S., & Duman, R. S. (2002). Brain-derived neurotrophic factor produces antidepressant effects in behavioral models of depression. *The Journal of Neuroscience, 22*(8), 3251–3261.
Smoller, J. W. (2016). The genetics of stress-related disorders: PTSD, depression and anxiety disorders. *Neuropsychopharmacology, 41*, 297–319.
Treur, J. (2016a). Dynamic modeling based on a temporal-causal network modeling approach. *Biologically Inspired Cognitive Architectures, 16*, 131–168.
Treur, J. (2016b). *Network orientated modelling: Addressing complexity of cognitive, affective and social interactions.* Springer Publishing.
Treur, J. (2018). *The ins and outs of network-oriented modeling: From biological networks and mental networks to social networks and beyond. Transactions on computational collective intelligence.* [in Press Paper for Keynote Lecture at ICCCI'18].