Utilization of a Virtual Patient Model to Enable Tailored Therapy for Depressed Patients

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Abstract. Major depression is a prominent mental disorder that has significant impact upon the patient suffering from the depression as well as on the society as a whole. Currently, therapies are offered via the Internet in the form of self-help modules, and they have shown to be as effective as face-to-face counseling. In order to take automated therapies a step further, models which describe the development of the internal states associated with depression can be of great help to give dedicated advice and feedback to the patient e.g. by means of making predictions using the model. In this paper, an existing computational model for states related to depression (e.g. mood) is taken as a basis in combination with models that express the influence of various therapies upon these states. These models are utilized to give dedicated feedback to the patient, tailor the parameters towards the observed patient behavior, and give an appropriate advice regarding the therapy to be followed.

Keywords: Virtual patient, depression, support agent, tailored advice.

1 Introduction

Major depression is currently the fourth disorder worldwide in terms of disease burden, and is expected to be the disorder with the highest disease burden in high-income countries by the year 2030 according to a prediction of the World Health Organization (WHO). Within mental health care, a new generation of therapies for treatment of depression has emerged, in which patients can use Internet-based self-help therapies. This takes away the long waiting times for psychological treatments and also removes the barrier of going to a doctor to seek counseling. A wide variety of therapies are available in the form of self-help modules, including activity scheduling (also called behavioral activation, see e.g. [14]), cognitive behavior therapy (see e.g. [3]), and problem solving therapy (see e.g. [10]). A growing number of randomized trials have been performed that show that such forms of treatment are as effective as face-to-face treatment (see e.g. [15]; [1]). However, these treatments currently do not provide very personalized or tailored support to the patient, which could potentially lead to an even better treatment of the depression.

In order to provide such personal advice and support, the supporting system (for instance in the form of a personal support agent) should be able to build up a picture of the current and potential future development of the patient, and the influence of the

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therapy upon this development. Based upon this picture, the system can determine how the patient is progressing and is expected to progress further, provide feedback on this, and also select the most appropriate therapy for the patient. In previous work [5], a computational model for the cognitive states associated with depression has been developed based upon literature available in clinical psychology, including elements such as *mood*, *thoughts*, and *appraisal* and their interrelationship. This model can be used to predict the development of these states of the patient over time. In extensions of the model (see [6];[7]), the influence of various therapies upon these states of the patient have been included, which enables predictions on the effectiveness of the therapy for the patient.

In this paper, an approach is presented which utilizes such models to provide dedicates feedback to the patient and give advice on the appropriate therapy to follow. This process is composed of three subparts: (1) deriving the therapy with the highest probability of success and providing this as advice to the patient, (2) once a therapy has been selected, the predicted trends can be compared with the observed trends of the patient to provide feedback, but also to trigger a process which evaluates whether there is potentially a more effective therapy than the current one, and (3) tuning the parameters of the predictive models towards the observations with respect to the patient in case large deviations are found to improve the accuracy of future predictions.

This paper is organized as follows. Section 2 briefly describes the underlying models. In Section 3 the algorithms that describe how such models can be utilized are described, whereas Section 4 presents simulations results for a dedicated scenario. Finally, Section 5 is a discussion.

2 Therapeutic Models

In [6] and [7], therapies are described in terms of a computational mood model [5]. In Figure 1, the mood model is shown in gray. This model uses situations in the world (*world events*) and personal characteristics such as *coping skills*, *vulnerability* and *prospected mood level* to describe the state of a person. In the figure, the black arrows and grey circles describe the therapeutic influence of the Cognitive Behavior Therapy (CBT) module with three effects on the mood model: *intervention*, *reflection* and a therapy-dependent effect, *appraisal* in case of CBT. The first two hold for all interventions.

- *Intervention* effect: the positive effect on the thoughts of a person when this person is following a form of therapy.
- *Reflection:* the learning effect of a therapy by increasing coping skills. The concepts involved in reflection differ among the therapies.
- Therapy-dependent effect: each intervention has its own view on how to treat depression. CBT focuses on changing the appraisal of a situation, the other two modeled interventions focus on introducing more pleasant (activity scheduling) or physical (exercise therapy) activities into a person’s daily life. These effects are described in more detail below.

The idea behind CBT is that there is a relation between how a situation is appraised (*appraisal*) and the mood level. During the therapy, one learns that emotions are triggered by thoughts about a situation (*appraisal*) rather than by the situation itself.

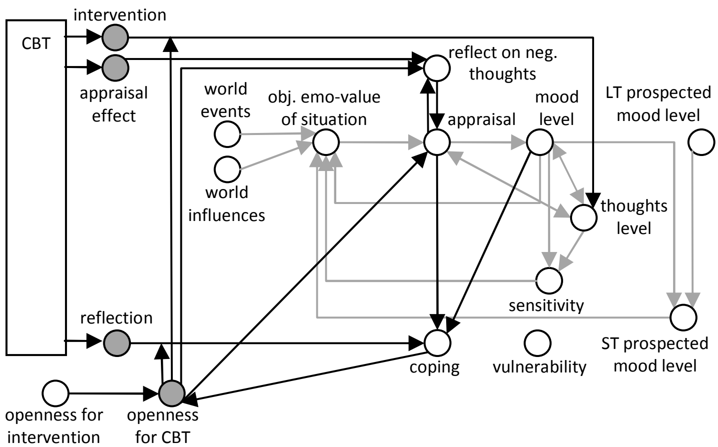

Fig. 1. Computational model for Cognitive Behavior Therapy (CBT). The model for dynamics of mood and depression is shown in gray. The additions for the CBT model are shown in black.

These negative thoughts can be identified and changed into thoughts that are more positive. This is modeled by an *appraisal effect* from the CBT module influencing the element *reflect on negative thoughts,* which in turn influences *appraisal*. Openness for CBT determines to what extent these concepts are influenced. A person that is very open to a specific therapy will put more effort into the therapy and will learn quicker.

The other therapies modeled in previous work are Activity Scheduling and Exercise Therapy. During Activity scheduling (AS), the patient learns the relationship between the selection of a relatively positive activity and the level of mood (i.e., when you do fun things, you will start to feel better, based on the reinforcement theory in [14]). In order to learn this relationship, the therapy imposes the selection of positive situations. Exercise Therapy (ET) is based on the idea that physical exercise may improve mood ([4], [8]). A number of concepts have been added to the model, such as *physical state* and *physical norm*. The physical state influences the mood level positively and learning the relation between these concepts increases the coping skills. For more details on the mood model and the models of the different therapies, see ([5], [6], [7])

3 Support System Utilizing Therapeutic Models

In order to utilize the models described in Section 2, this Section introduces a three stepped approach. The first step comprises of the utilization of the models to advise the patient which therapy to follow. Once a therapy has been selected, comparisons can be made between the predicted developments of the patient in terms of the mood level and the actual development of the patient based upon measurements. This can either be used as a basis for feedback (e.g. "*you're developing much faster than expected, congratulations!*") or to trigger a new process to see whether a switch in therapy could result in a more speedy recovery. In case the predictions of the model show to be inaccurate, the third step is to perform parameter adaptation to improve the predicative power of the models. Each of these elements is treated in more detail below.

3.1 Selecting a Suitable Therapy

When a patient wants to start with a treatment, the first step to undertake is to determine what type of therapy the patient should follow. In the approach presented in this paper, the models which describe the development of internal states and the influence of therapy upon this development are utilized to advice the most appropriate therapy. Simulations are performed to see how the mood of the patient will develop, given a certain therapy which has been selected. In these models, a number of parameters are present that depend on the characteristics of the patient (as described in Section 2). Specifically, the following parameters are assumed to be set in accordance with such patient dependent characteristics:

1. Initial level of mood
2. Coping skills level
3. Vulnerability level
4. Openness for the type of therapy

Hereby, the first element (initial level of mood) can be measured directly ("*what is your mood on a scale from 1-10?*"), whereas the second and third parameter (i.e. coping and vulnerability) follow from a set of dedicated questions that are part of an initial questionnaire the patient has to fill in. The parameter openness for therapy depends on the prior experience of the patient (has the therapy been followed before, and if so, was it successful), and the general characteristics (e.g. does the patient like to run to determine whether the patient is open towards exercise therapy). Once precise values are derived for each of these elements, predictive simulations for each of the different therapies can be run. The criterion for advising the best therapy is simply the therapy in which the mood level will be 6 or higher during three consecutive days (i.e. sufficiently high again) within the shortest time span. If none of the therapies meets this criterion, the therapy with the highest mood level at the end of the therapy is advised.

3.2 Comparing Predictions and Actual Observations

Once the patient has decided to follow a certain therapeutic module, the support agent can monitor the effectiveness of the therapy by comparing the predictions of the models with the actual observations around the patient. Such a comparison is not a trivial task. A precise comparison between the predicted and observed values is often difficult to do, as one more wants to see whether the trends are similar, not whether the precise numbers are the same. Therefore, first trends are expressed within the development of the states of the patient which are applicable to both the predictions using the model and the actual observations of the patient. Thereafter, these trends are compared and conclusions are drawn, possibly resulting in actions being undertaken.

Identification of Trends. Making a comparison between the data which has been collected from the patient (e.g. due to the mood ratings the patient has performed) and the predictions of the model is difficult. The model tends to make predictions that are relatively smooth and give a more general indication of the trends of the patient, whereas the observations around the patient are fluctuating a lot more, for instance during the start of the day the mood is generally rated a lot lower compared to the middle of the day. As a consequence, a comparison based upon the general trends of the predictions of the model and the general trends in the observed data of the patient is much more useful. The following trends are hereby distinguished:

- *Increasing during a period x:* The general trend is that a particular aspect of the therapy or state of the patient is increasing during a certain time period x.
- *Decreasing during a period x:* The general trend is that a particular aspect of the therapy or state of the patient is decreasing during a certain time period x.
- *Stable (fluctuations within certain boundaries) during a period x:* The general trend for a particular aspect of the therapy or the state of the patient is stable during a period x.
- *Average over a period x is above a threshold th:* The average value for a particular aspect of the therapy or the state of the patient is above a certain threshold value th during a certain time period x.
- *Average over a period x is below a threshold th:* The average value for a particular aspect of the therapy or the state of the patient is below a certain threshold value th during a certain time period x.

All of these trends are expressed in more detail below.

Variable v increasing during a period x.
In order to express increasing trend with respect to some measurements around the patient is not a trivial matter. Certain outliers might occur in the data that need to be filtered out, and when looking at individual measurements such outliers can be quite difficult to detect. For instance, sometimes a clear increasing trend can be seen, but rare outliers prohibit a strict property with respect to an increasing measurement from being satisfied. Of course, many different techniques can be applied to detect the increasing trends, e.g. the fitting of a linear curve through the data making use of the method of least squares (e.g. [13]). In this case, another approach has been used which averages the measurements over the days and detects whether these averages are monotonically increasing. Due to the fact that the predictions as given by the models provide quite a lot of data per day, this approach is computationally more efficient, and is also closer to the current approaches used in clinical psychology. The algorithm to derive whether this criterion is indeed fulfilled is expressed on the next page. Note that hereby a start and end time are assumed. The duration between these time points should be equal to x (the duration expressed in the property).

In the algorithm, a loop is present in which the average is taken for a window from the current time point till the current time point plus a duration d (the window size).

In case this average is strictly higher than the average in the previous window, the property can still be satisfied, and the loop continues by setting the current time to a new value. In case the loop is completely passed the property succeeds. If a case occurs whereby the average is not higher than the previous average, the property fails and the cycle ends.

Algorithm 1. *Increasing trend from start time t_{start} to end time t_{end}*

```
t_current = t_start
previous_average = 0;
while (t_current < t_end) {
        total = 0;
        for (int i=0; i < d; i++){
                total = total + v(t_current + i);
        }
        current_average = total / d;
        if (current_average ≤ previous_average) {
                return false;
        }else{
                previous_average = current_average;
                t_current = t_current + d;
        }
}
return true;
```

Variable v decreasing during a period x

For the decreasing trend, a similar approach can be taken as described for the increasing trend.

Variable v stable (fluctuations within certain boundaries) during a period x

Furthermore, a stable trend is also expressing, which indicates that the variable v fluctuates within certain boundaries.

Algorithm 2. *Stable trend from start time t_{start} to end time t_{end}*

```
t_current = t_start
average = 0;
total = 0;
timesteps = 0;
for (int t=t_start; t < t_end; t++){
        timesteps++;
        total = total + v(t)
}
average = total / timesteps;
for (int t=t_start; t < t_end; t++){
        if (v(t) > (1+b) * average || v(t) < (1-b) * average){
                return false;
        }
}
return true;
```

Hereby, once a value exists which deviates more than *b* from the average value during the entire period, the algorithm returns false.

Average of variable v over a period x is above/below a threshold th.
For the sake of brevity, the algorithm underlying this definition is not shown, but for a calculation of the average value algorithm 2 can be followed, and a simple check can be performed to see whether this average is above or below the threshold value th.

Comparison of Trends. Once the trends for both the actual patient states and the predicted patient states are known, a comparison can be made to see how these trends relate to each other. In this case, a comparison is based upon the general level within the patient (the patient is doing well when the average level is above six) as well as the trend in the development of the measurement (i.e. stable, increasing or decreasing). In Table 1 a categorization is given of the comparison between the predicted and observed trend regarding the development of the patient.

Table 1. Comparison between trends

	Predicted trend	good			bad		
Observed trend		increasing	stable	decreasing	increasing	stable	decreasing
good	increasing	o	+	++	++	++	++
	stable	-	o	+	+	+	++
	decreasing	--	-	o	o	o	o
bad	increasing	o	o	o	o	+	++
	stable	--	-	-	-	o	+
	decreasing	--	--	--	--	-	o

In the table, a '--' expresses a significant worse development of the patient's state compared with the predictions. A '-' indicates a somewhat worse development, and a 'o' represents a development comparable with the prediction. '++' is a far more positive development, whereas '+' is a somewhat more positive development. In all cases, except when the patient is performing significantly worse, feedback is given to the patient how he/she is doing compared with the predictions. All of these messages are phrased positively and meant to stimulate the patient as much as possible. Examples of such messages include: "*you're doing much better than other people in your situation, keep up the good work!*" for the case of '++' and "*you're progression is a little bit less than expected, try as best as you can to get the most out of the therapy and enable a rapid recovery!* ". If the performance is significantly worse than expected, a process is started to seek for an alternative therapy which might be more suitable for the patient. The first step in this process is to tune the parameters of the models used to predict the patient development towards the observed data of the patient.

3.3 Tuning the Model towards Observed Patient Behavior

Once it has been shown that the trend in the patient state is much worse than expected, apparently the predictions of the models were not sufficiently accurate. Hence, the parameters of the models should be adapted such that the model describes the behavior of the patient more precise. Thereafter, the models can again be utilized to select the most appropriate therapy (cf. Section 3.1) with these newly gained insights about the parameters of the patient. In the parameter adaptation process, two parameters are adapted, namely coping and vulnerability. For the openness of therapy the old value is assumed (as it has developed as a result of the model), and for the initial level of mood the actual input of the patient is used. Algorithm 3 expresses the algorithm for the parameter adaptation process.

Algorithm 3. *Parameter adaptation*

```
current_best_value_coping = low;
current_best_value_vulnerability = low;
current_best_mse = 1; // maximum value

for all settings for coping
        for all setting for vulnerability
                current_mse = mse(current_value_coping, current_value_vulnerability,
                                        current_therapy);
                if (mse(current_mse < current_best_mse) {
                        current_best_mse = current_mse;
                        current_best_value_coping = current_value_coping;
                        current_best_value_vulnerability = current_value_vulnerability;
                    end
        end
end
```

The mean squared error is used as a measure of the fitness of the parameters. Furthermore, a limited set of parameter values is assumed to avoid a too high computational load. Once the ideal parameters have been selected, the different alternative therapies can again be compared, following the approach described in Section 3.1. Hereby it is assumed that the previous values of all the states are taken as an initial value when starting the run the predictions.

4 Simulation Results

In this Section, the overall approach is evaluated by means of simulation runs with a typical patient. The figures below show the different steps of one simulation of a person with low coping skills, high vulnerability, a low initial mood level and medium openness to therapy. The first step of the support system is to select a suitable therapy. Figure 3 shows the predicted mood level given the parameters above for the therapies AS, CBT and ET. The advice given to the person is to follow exercise therapy, because a sufficiently high mood level is reached within the shortest time span (52 days for ET, 59 days for AS and 53 days for CBT). In the figure, the solid black line indicates the threshold for the patient state in order to be considered sufficiently high.

Following step 2, the situation is evaluated after week 7 of the exercise therapy. In Figure 4a, the actual patient state, based on the reported mood level, is shown as a solid blue line. The predicted state of the patient is shown as a red striped line. The trends are depicted as a circle for the virtual and an asterisk for the actual trend, where a value of 1 means increasing, 0.5 means stable and 0 means decreasing. The trend of

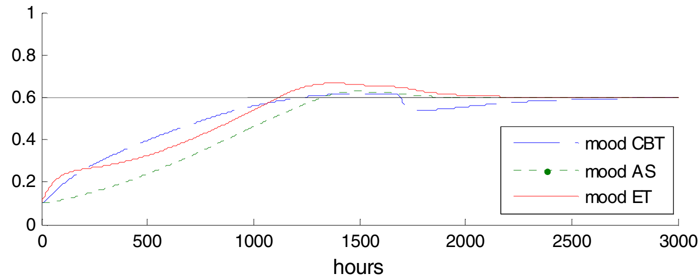

Fig. 3. Predicted mood levels for the three therapies

the prediction (red circle) is good and increasing whereas the actual trend is bad and decreasing (blue asterisk). According to Table 1, this situation is undesirable and the parameter adaptation process is started as step 3 of the support system.

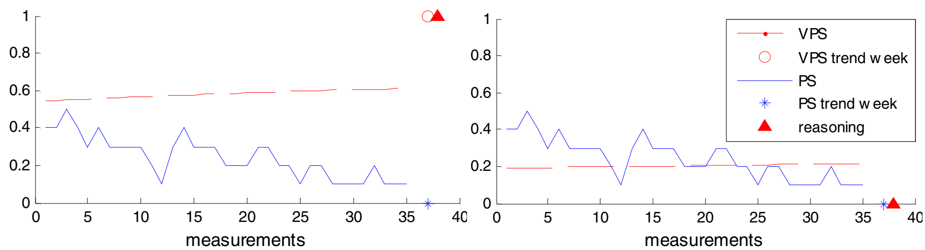

Fig. 4a, b. Virtual vs. actual patient state in week 7 of ET before (left) and after (right) parameter adaptation

Running algorithm 3 results in a new set of parameters describing the current state of the patient more precisely. The predictions based on the new parameters are shown in Figure 4b. The best fitting coping skills level is very low, in combination with a very high level of vulnerability. The mean squared errors for the coping levels very low, low, medium and high in combination with opposite vulnerability levels are respectively: 0.02, 0.13, 0.19 and 0.30. Combining corresponding levels for coping and vulnerability lead to even greater mean squared errors.

Since the patient is not doing very well (the patient state trend is bad and decreasing), the support system can now start with step 1 again: selecting a suitable therapy. All therapies are simulated again to see if the patient is better of switching to a different therapy. It is assumed that switching to a different therapy is experienced as positive, due to the personal advice that is given. Therefore, the simulations of the other therapies than the current start with a mood level one point higher than the last reported mood level. Figure 5 depicts the mood levels of the three therapies given the current state of the patient and the newly determined parameters. The support system advises to switch to CBT, because it is expected that CBT leads to the highest mood level at the end of the therapy.

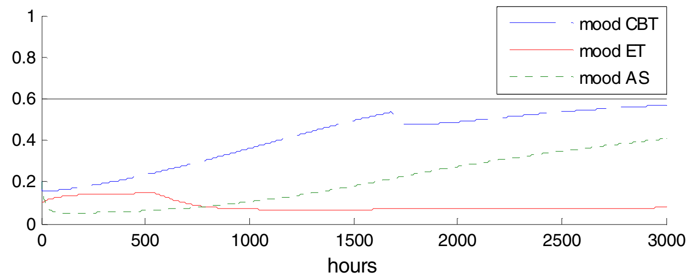

Fig. 5. Predicted mood levels for the three therapies

5 Discussion

In this paper an approach has been presented to provide feedback and give personalized advice to people suffering from a depression. In order to come to such an approach, cognitive models which represent the states associated with depression are utilized, in combination with extensions expressing the influence of dedicated therapies upon the mental states of a human. The presented approach consists of three main elements: (1) the utilization of the models to make predictions of effectiveness of therapy and give advice on the therapy with the fasted expected recovery, (2) the comparison of the predictions using the models with the actual observed behavior to provide feedback to the patient and potentially trigger a process to advise a therapeutic change, and (3) the tailoring of the parameters of the models towards the behavior of the patient in case this is necessary to guarantee the accuracy of the predictions. The overall approach has been evaluated by means of simulations runs, and shows that the approach indeed works as expected. Next steps include the validation of the models themselves with empirical data, after which the presented approach will be deployed as part of a system to be tested with actual patients.

Within the literature, several computational models incorporating emotions have been presented. For instance, [2] presents an example model which involves emotions and the influence thereof upon the behavior of an agent. Other examples of models include [9] in which agents are programmed that involve emotions in their deliberation process, and many more exist. In this paper, the utilization of these models is taken one step further, namely to give advice based upon predictions using these models. With respect to the identification of trends in the development of the patient (which is a necessity to make a comparison possible) as a first step a method has been selected which is close to the current approach followed by therapists, but more advanced computational methods could be utilized. Furthermore, for the parameter adaptation an exhaustive search approach based upon a limited set of allowed parameter values has been selected to guarantee the robustness of the model as well as to avoid overfitting. Of course, the disadvantage is that large discrepancies can still be present. Therefore, for future work, more advanced parameter adaptation techniques will be used, for instance using more mathematical-based approaches (see e.g. [12]) or Artificial Intelligence learning techniques such as Genetic Algorithms (see e.g. [11]).

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