Outline of an Action-Oriented Classification of Mental Disorders: A Hypothetical Model

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Abstract: The outline of an action-oriented classification of mental disorders is mainly theoretically proposed. Based on the discussion and interpretation of the "Schichtenregel" (three-layer-rule) by the German psychiatrist Karl Jaspers, a synaptic model is elaborated for the pathophysiology of depression, mania and schizophrenia. According to a logic of balance, synapses may be balanced, underbalanced (depression), overbalanced (mania), or unbalanced (schizophrenia). From a psychological point of view, patients with a major depression are hyperintentional, patients with mania are hypointentional, and in the case of schizophrenia they are dysintentional. Decisive in the synaptic model proposed is the number of receptors for neurotransmitters expressed in the membranes of astrocytes. A normal or disturbed balance of behavior can be described as variables of the intentional programs and as values of the description of their feasibility. This enables a computer supported classification of an action-oriented diagnostic manual. The future realization of this procedure may improve psychiatric research and especially clinical practice.

Keywords: Mental disorders, synaptic imbalance, disordered intentionality, therapeutic feasibility, classification.

INTRODUCTION AND HYPOTHESIS

Supposing that every theory of action should show how human intentional programs can be realized based on appropriate actions, we essentially deal with the principle of feasibility [1]. Therefore, I start out with an attempt to apply this principle of feasibility to the classification of mental disorders.

First of all, the current diagnostic manuals are valuable, especially as a "system of reference" [2]. However, we should be aware of the fact that the statistical limitations of various classification systems often lead to an unexact diagnosis not corresponding to the clinical impression of the individual patient. In some cases the diagnosing person is challenged with a "free play" of interpretation [3]. Most importantly, a diagnosis represents a clear advice on how to improve or even heal a disorder [4].

My hypothesis is as follows: a mental disorder occurs if an intended or necessary action cannot be realized temporarily or permanently, or (and) if it must be realized permanently. This behavior exerts destructive effects since it does not correspond to the real intentions of a person. It follows that all persons diagnosed as mentally ill in the broad sense suffer from problems to act, at least in relation to the environment. Thus, all mental disorders can be deduced from action problems.

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Action-Oriented Discussion and Interpretation of the "Three Layer Rule" (Schichtenregel) of Jaspers' Psychopathology as an Example

The classification of mental disorders dates back to Griesinger and has been elaborated by Jaspers [5] in his "Schichtenregel" (three layer rule). Accordingly, the first layer comprises the exogenous psychoses caused by organic impairment. The second layer describes the endogenous psychoses of which we presently possess more information, but their psychopathology still remains unknown. The third layer includes all psychic disorders which Jaspers qualified as variants of normal behavior. However, up to now the diagnostic manuals provide hardly any therapeutic devices.

As a consequence, we should particularly analyze in which area or domain the capability of the patient to act appropriately is impaired. Here, we need a questionnaire that comprises all areas in which the patient is able to act appropriately. For instance, we can only improve the quality of life of a patient with dementia if we test his/her intentional potential and attempt to provide its realization accordingly.

However, in the cases of major depression, mania and delusions (schizophrenia), we are challenged with the different qualifications of the action potential [6]. Thus, depression may be determined by a "hyperintentionality" (to intend too much). Especially patients with chronic depression may suffer from the feeling of non-feasibility of some or all subjective intentions. Often some kind of compensation of one or more non-feasible actions by a permanent "must do" occurs. The latter exerts destructive effects and is in

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the current diagnostic manuals mostly qualified as a comorbidity [7]. In contrast, patients with mania spontaneously act according to their flooding of ideas. Here, the so-called flight of ideas can be interpreted as an expression of the incapability to generate feasible action programs, coined as hypointentionality [8]. In addition, the conviction of these patients that they can do anything represents a kind of "pseudoomnipotence" [9] which mostly exerts very destructive effects [10].

A patient suffering from a chronic delusional disorder (paranoia, schizophrenia) experiences the world as a "general case", since his/her brain may embody a universe that cannot differentiate between the inner and outer specific realities. It follows that in intersubjective communication the individualities of other persons cannot be recognized. We also notice a dysintentionality in the communication with these patients [11]. Therefore, it is impossible for the patient to really cooperate or even generate a common product in the broad sense. Importantly, these patients accept the gift of various things for the maintenance of a modest quality of life. This is the constructive action-oriented approach of social psychiatry.

What psychic disorders classified by Jaspers as abnormal variants of normal behavior concerns, it is rather difficult to elaborate an action-oriented diagnosis. First of all, an action-oriented analysis of the realization of intended action programs and its disorders is necessary. Based on such analyses advices on how to act or to structure every day life are possible. In many cases a kind of "circular thinking" impairs the coping with duties of daily living. Therefore, we should attempt to structure the behavior according to a feasible action program. If we are able to propose a feasible and simple action program, the patient can stepwise reject all his/her non-feasible ideas and problems and realize the intentions by means of appropriate actions. Such a therapeutic approach to non-psychotic psychic disorders may exert constructive effects towards a restitution of disordered behavior.

Although a discussion of various therapeutic approaches in this context would also be of interest, I will merely attempt to outline synaptic models of depression, mania and delusions (schizophrenia) serving as a biological basis for action-oriented diagnostics and classification.

SYNAPTIC MODELS OF THE PATHOPHYSIOLOGY OF AFFECTIVE DISORDERS AND SCHIZOPHRENIA

Since computer programs can exert a progress in the classification of mental disorders, let me start out with a description of a formal principle based on an action-oriented classification.

Logic of Balance

The formalism applied is the logic of balance which has been introduced by the German-American philosopher Guenther [12]. The proposition is that the operations of a living system are balanced if the number of variables and values are equal. Generally, a variable is defined as anything able to vary but taking no more than one value at a time. It is an ambiguous name of any one of a class of things (range of variables) where the members of the class are the values of the variable [13]. From a biocybernetic point of view, a variable is something that retains its own identity while capable of changing its state in the sense of material realization [14]. Based on this latter definition, one can also say that variables in a living system "strive" for their feasibility with values in the sense of appropriate materials.

There are principally four system states of feasibility possible. First, the number of variables (*n*) and the number of values (m) is equal (m=*n*). Second, the

Table 1: Logical Balance, Overbalance and Underbalance in Tripartite Synapses

		Glial receptors (variables)					
	m / n	1	2	3	4	5	6
neurotransmitters (values)	1	**1** **1**	2 1	3 1	4 1	5 1	6 1
	2	1 2	**2** **2**	3 2	4 2	5 2	6 2
	3	1 3	2 3	**3** **3**	4 3	5 3	6 3
	4	1 4	2 4	3 4	**4** **4**	5 4	6 4
	5	1 5	2 5	3 5	4 5	**5** **5**	6 5
	6	1 6	2 6	3 6	4 6	5 6	**6** **6**

This matrix shows the glial receptors (variables, *n*=6) and six neurotransmitters (values, *n*=6). In each number pair the upper number designates glial receptors, the number below neurotransmitters. According to the logic of balance, the system is balanced if the number of variables (glial receptors) and the number of values (neurotransmitters) is equal. The number pairs (in squares) in the diagonal of the matrix (1…6) represent balanced tripartite synapses. The number pairs above the diagonal designate underbalanced synaptic systems, since the glial receptors outnumber the neurotransmitters. In contrast, the number pairs below the diagonal represent overbalanced tripartite synapses, because the neurotransmitters outnumber the glial receptors.

variables outnumber the values (*n*>m). This system is underbalanced, since the variables do not have enough values (material) available for their realization. Third, the values outnumber the variables (m>*n*). This system is overbalanced because of an excess of material. Fourth, the system is totally lacking of variables and, therefore, thoroughly unbalanced.

Possible Role of Synaptic Imbalances for the Pathophysiology of Endogenous Psychoses

Figure **1** outlines the function of a balanced tripartite synapse, since the number of glial receptors and the amount of cognate neurotransmitters is appropriate. This situation also holds for the other receptor locations. Neurotransmitters (NT) released from the presynapse occupy the postsynaptic receptors (poR). In parallel, NT occupy the glial receptors (glR) on the astrocyte (Ac), activating the production of gliotransmitters (GT) within the Ac. The GT are released in the synaptic cleft occupying the presynaptic receptors (prR) in the sense of a negative feedback. In addition, the occupancy of postsynaptic receptors directly depolarizes the neuron. This glial function temporarily turns off synaptic information processing and neurotransmission can start again. In this model of a tripartite synapse, I focus on the active role of glial receptors and the negative feedback mechanism exerted by gliotransmitters. Receptors on astrocytes are meanwhile identified for the various neurotransmitters [15]. The same holds for the identification of transmitter substances produced by astrocytes called gliotransmitters [16] and the identification of cognate presynaptic receptors [17].

All of the above suggests a straightforward hypothesis: underbalanced tripartite synapses may cause the pathophysiology of depression, overbalanced tripartite synapses may be responsible for the pathophysiology of mania, and unbalanced tripartite synapses may underly the pathophysiology of schizophrenia.

Before describing the synaptic models of these disorders, the formal basis of the functions of neurotransmitters and glial receptors in tripartite

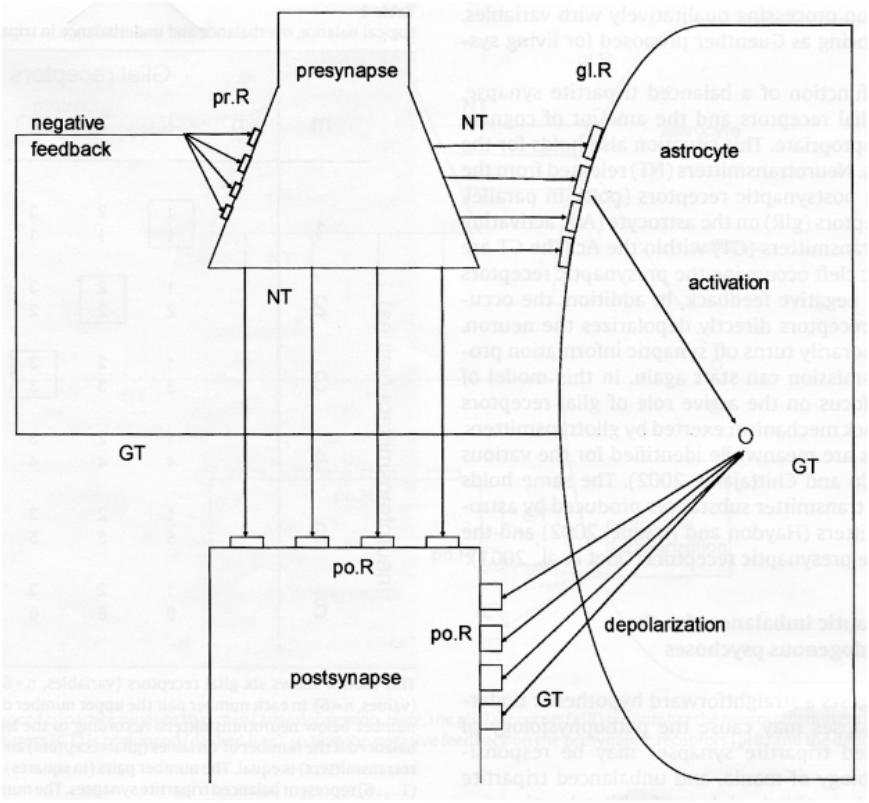

Figure 1: Model of a balanced tripartite synapse.

According to the logic of balance, the number of neurotransmitter (NT) and the number of the glial receptors (glR) is equal. For the sake of clarity, neuromodulators, ions, etc. are omitted. NT released from the presynapse occupy postsynaptic receptors (poR). In parallel, NT occupy glR, activating the production of gliotransmitters (GT). GT are released from the astrocyte into the synaptic cleft and they occupy the presynaptic receptors (prR) in the sense of a negative feedback and also depolarize postsynaptic receptors. This glial function leads to a temporary turn off of synaptic information processing and neurotransmission can start again.

synapses should be shortly elaborated for a better understanding of the hypothesis. Table **1** shows the logical balance or imbalance between glial receptors (variables, *n*) and neurotransmitters (values, m). On the horizontal line of this matrix the glial receptors are enumerated (*n*=*6*), on the vertical line the neurotransmitters (m=*6*). Within the matrix the upper number designates the glial receptors, the lower one the neurotransmitters. The number pairs in squares building the diagonal represent balanced tripartite synaptic systems. The number pairs below the diagonal are overbalanced, since the neurotransmitters dominate the glial receptors. In contrast, the number pairs above the diagonal represent underbalanced tripartite synaptic systems dominated by the glial receptors. Not shown is an unbalanced system. This is the case if a synaptic system is incapable of producing functional glial receptors in the sense of a total lack of variables [18]. Next, the pathophysiology of depression, mania and schizophrenia will be deduced from the proposed physiological and formal synaptic model.

Depression

The core symptoms of depression are depressed mood, diminished interest or pleasure, disturbances of circadian rhythms, psychomotor disturbances (retardation or agitation), feelings of insufficiency (worthlessness etc.) [19]. How could an underbalanced tripartite synapse be explanatory for the pathophysiology of these symptoms of depression? As hypothesized above, if the receptors on astrocytes are increased such that a relative lack of neurotransmitters arises, then such an underbalanced tripartite synaptic system may be responsible for depression on the behavioural level. Figure **2** depicts an underbalanced tripartite synapse. Because most of the effective treatments of mood disorders were discovered by empiricism, the effectiveness of somatic treatment has propelled neurotransmitter theories rather than *vice versa* [20]. My approach is contrary to this trend by deducing the pathophysiology of endogenous psychoses from a theoretical model. Supposing that not only the excess of glial receptors but also the relative lack of

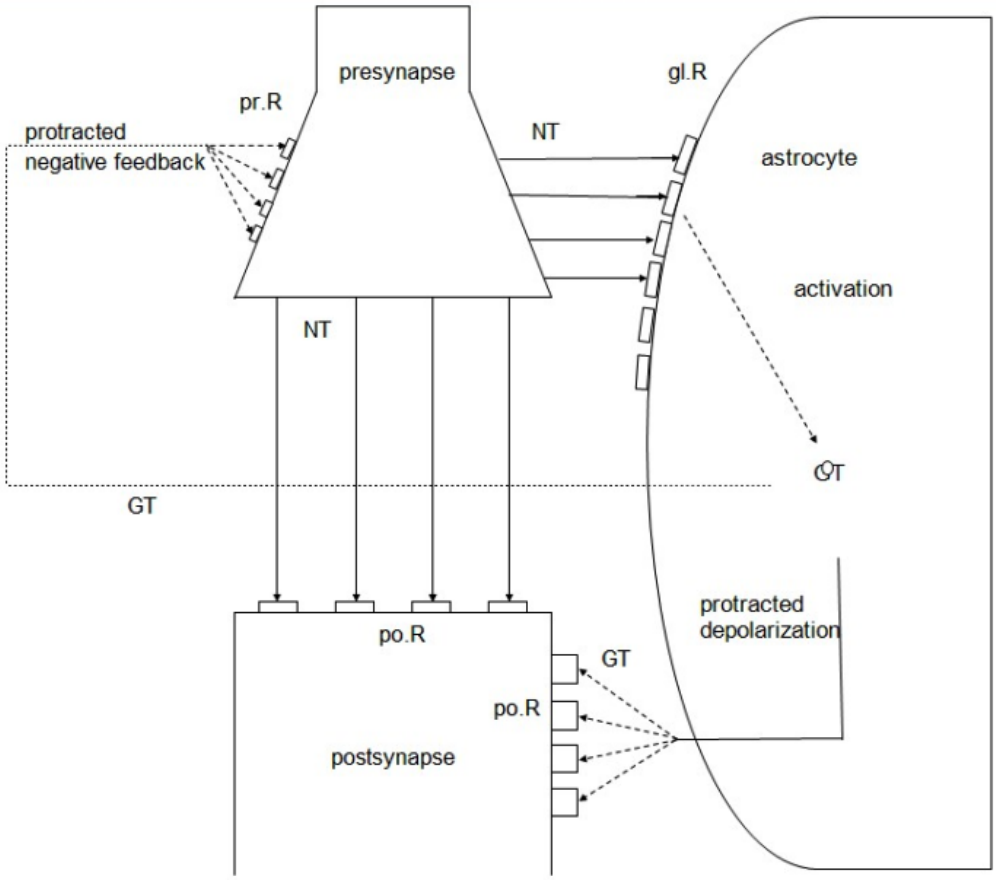

Figure 2: Model of an underbalanced tripartite synapse that may cause depression.
Here, the glial receptors (glR) outnumber the neurotransmitters (NT). Therefore, the activation and production of gliotransmitters (GL) is prolonged (dashed line), so that the negative feedback on the presynaptic receptors (prR) and the depolarization of the postsynapse is also protracted.

neurotransmitters in the synaptic cleft is responsible for depressive mood, it is conceivable that a treatment with reuptake inhibitory substances could be successful. Most importantly, according to my model of depression, the increased concentration of neurotransmitters in the synaptic cleft may lead to a balance of synaptic information processing *via* a sufficient occupation of glial receptors.

The biogenic amine hypotheses of depression postulate a deficiency of biogenic amines in synapses [21-23]. In this context, it should be mentioned that brain diseases such as Parkinson's disease also show a lack of transmitters in pertinent synapses, but this is not necessarily accompanied by a depressive mood [24]. Hence, depression may arise only if the glial system is also affected in the sense of an underbalanced tripartite synaptic system.

Mania

The core symptoms of mania are elevated mood, irritability, flight of ideas, grandiosity and insomnia [19]. These clinical features of mania are generally the opposite of those of depression. Figure **3** shows schematically an overbalanced tripartite synapse that may cause mania. Here the number of glial receptors is decreased so that these receptors are "overloaded" with neurotransmitters. This system state may lead to a fastened production of gliotransmitters within the astrocytes (fat line) and shorten the cycles of negative feedback on the presynaptic receptors (fat arrows) and to a rapid glial depolarization of the postsynaptic neuron. Such overbalanced tripartite synapses could be responsible for the high manic irritability as well as flight of ideas and motor hyperactivity.

From a psychological point of view, patients with mania are absolutely convinced that every thought or idea is immediately feasible. In other words, they have no problems to realize any intention, so these patients are actually hypointentional. There is no striving or testing since all seems to be possible and appropriate [8]. Dependent on the transmitter systems or brain areas affected, the synaptic overbalance could cause the typical manic symptoms of euphoria and feelings of omnipotence. In addition, the rapid synaptic cycles

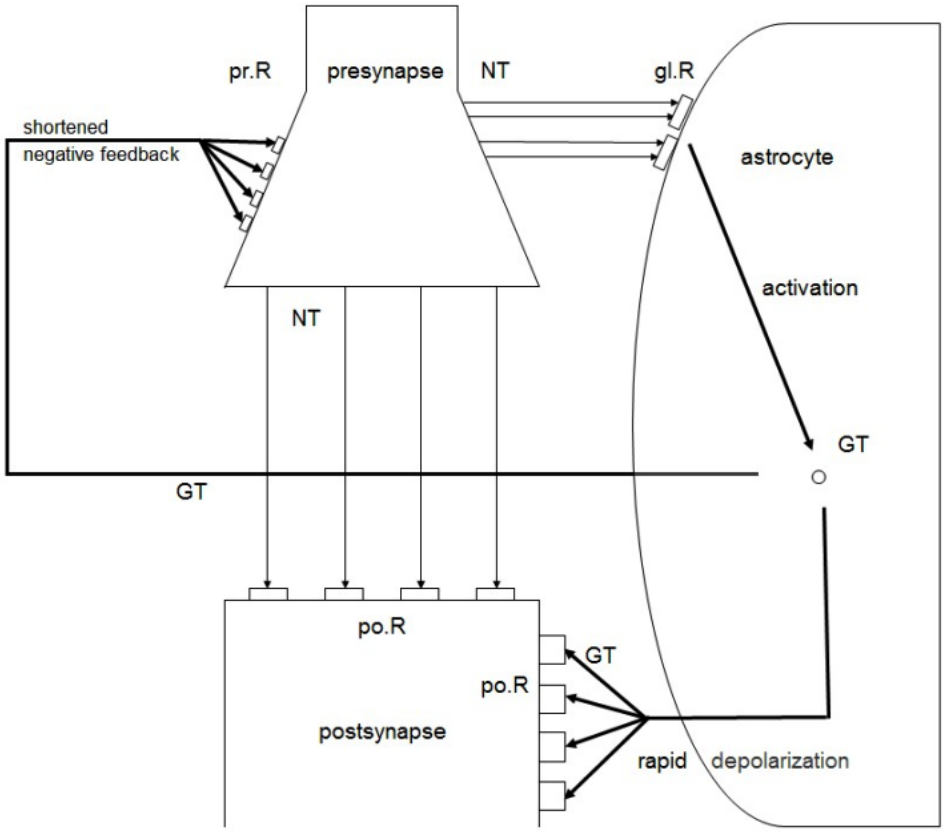

Figure 3: Model of an overbalanced tripartite synapse that may cause mania.
The number of glial receptors (glR) is decreased relative to the number of neurotransmitters (NT) leading to an "overoccupation" of glR by NT. Therefore, the activation and production of gliotransmitters (GT) may be fastened (fat line) and the cycles of the negative feedback and depolarization of the postsynapse are shortened (fat arrows).

could be explanatory of the manic distractibility, flight of ideas, hyperactivity and circadian disturbances, especially insomnia. Since the ideas of grandiosity are not feasible, I speak of manic pseudo-omnipotence [9].

Mellerup and Kristensen [25] hypothesize that mania may be caused by a dysfunction of reentry. According to Edelman and Tononi [26], reentry is a process of ongoing parallel and recursive signalling between separate neuronal groups along parallel reciprocal fibers that link these groups anatomically. Reentry alters the activity of the target areas it interconnects until a synchronous activity across these areas is created, which may be the direct biological mechanism of consciousness. Reentry may be faster in mania, specifically what the repetitive recursive signalling concerns, hereby allowing reentry to produce a conscious state faster than usually [25]. If one interprets negative feedback loops as a kind of reentry on the synaptic level, then the fastening of negative feedback in mania is in some aspects comparable to the hypothesis of dysfunction in reentry in neuronal networks.

The biological treatment of mania focuses on a reduction of the excess of neurotransmitters in the synaptic cleft. This seemingly leads to a normalization of information processing, because the occupancy of the glial receptors appears to be balanced. However, the underexpression of glial receptors may not be influenced by this treatment, so that after clinical remission of a manic episode hidden symptoms such as loss of motivation, loss of interests and anhedonia still may persist. This state is often misinterpreted as a depressive reaction to the manic behavior. Hence, a real remission may occur only if the genetically determined imbalance of the glial-neuronal interaction in tripartite synapses is resolved.

Mixed Manic-Depressive Episodes

Momentary tearfulness, depressed mood, and even suicidal ideation are commonly observed at the height of mania or during the transition from mania to retarded depression. Another common mixed feature is racing thoughts in the context of retarded depression. Mixed episodes proper are characterized by dysphorically excited moods, anger, panic attacks, pressured speech, agitation, suicidal ideation, severe insomnia, grandiosity, and hypersexuality, as well as persecutory delusions and confusion [27].

If a patient shows these depressive and manic symptoms at the same time, it seems likely that neurotransmitter systems in some brain areas are underbalanced while at the same time overbalanced in other brain areas. In that case it should be possible to attribute symptoms to the type of transmitter or glial receptors affected. Considerations about a possible pathophysiology of depression and mania in tripartite synapses should also be valid in mixed episodes. Because we presently do not know which synaptic systems are overbalanced and underbalanced, the treatment of mixed manic-depressive episodes is difficult, comparable to a trial-and-error procedure.

Schizophrenia

The core symptoms of schizophrenia can be divided into positive and negative symptoms, with the former including hallucinations, delusions, and disorganization, and the latter including anergia, flattening of affect, and poverty of thought content accompanied by significant disturbances in cognitive function [28]. Hypotheses concerning the etiology of schizophrenia comprise biological, psychological and sociological approaches [29-31]. Generally one can explain delusions and hallucinations in terms of a “loss of ego- or self-boundaries in the sense of an inner/outer confusion” [32-34].

Let me attempt to show how it may be possible to deduce the main schizophrenic symptoms from an unbalanced tripartite synapse. If the glial receptors are totally non-functional and therefore cannot be occupied by neurotransmitters, the system is unbalanced. As in Figure **4** depicted, the glial receptors (glR) are non-functional (crosses) and cannot be occupied by neurotransmitters (NT), so that the activation of the gliotransmitters (GT) is impossible. Hence, they cannot negatively feedback to the receptors on the presynapse (prR) and are unable to depolarize the postsynaptic neuron. As a consequence, the glia lose their inhibitory or boundary-setting function and the neural transmitter flux is unconstrained, as the flux of thought on the phenomenological level.

My brain theory is essentially based on the experimentally supported hypothesis that the glial system in its interaction with the neuronal system generates glial-neuronal compartments in the sense of specific functional units or operational domains [35, 36]. The interactional structure of an astrocyte with n-neurons can be defined as an elementary compartment of nerve cells. By simultaneously activating and deactivating neurotransmission in all of the synapses enveloped by an astrocyte, the astrocyte calcium wave

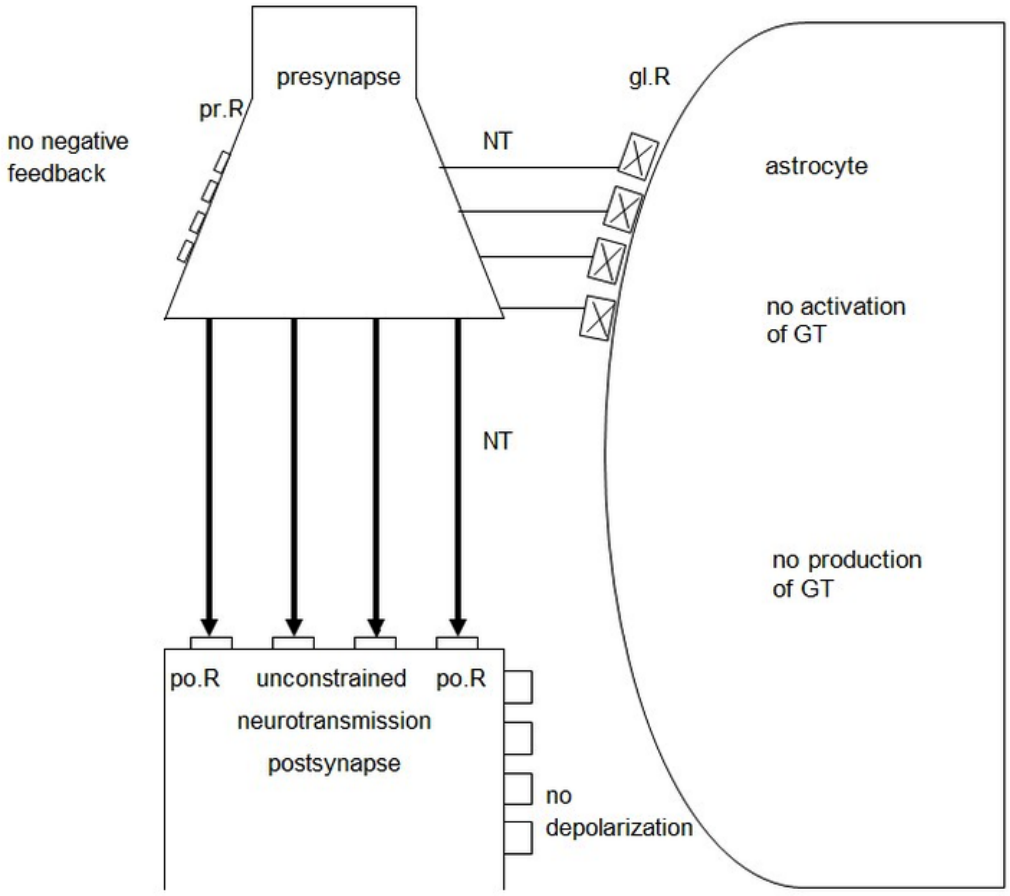

Figure 4: Model of an unbalanced tripartite synapse that may cause schizophrenia.
Non-functional glial receptors (glR), depicted by crosses, cannot be activated by neurotransmitters (NT). Since the activation and production of gliotransmitters (GT) is not possible, glia do not negatively feed back to the presynaptic receptors (prR) and cannot depolarize the postsynaptic neuron. This severe synaptic disturbance leads to an unconstrained neurotransmission (fat arrows).

may coordinate synapses into synchronously firing groups [37, 38], interpretable as harmonization [39].

One may argue that a glial determination of neuronal networks into functional units is not necessary because the neuronal system is compartmentalized *per se* [40]. However, according to my view, there is a qualitative difference between the purely neuronal compartments and the glia-determined compartments. Neuronal compartments may be merely functional for information processing, whereas glial-neuronal compartments may in addition have an information-structuring potency that we need for recognizing the qualitative differences between objects and individuals in our environment. That capacity may be lost in schizophrenic patients. Therefore, one can also speak of a loss of conceptual boundaries in schizophrenia.

The logic of balance enables to formally contribute both intentions and data of intentional programs to variables and values. The variables comprise the intentional programs and the values describe the themes or realms of feasibility, a disorder conceptualized for an action-oriented diagnosis, and, consequently, a therapeutic prescription on how and where to act in an intended and feasible mode.

COMPREHENSIVE BEHAVIOURAL ANALYSIS OF PATIENTS WITH A PSYCHOBIOLOGICAL DISORDER

We have constructed a questionnaire entitled "Salzburg Subjective Behaviour Analysis" (SSBA) [41] which assesses possible extreme displacements of the normal distribution and frequency of human modes of behaviour (i.e. work, sleep, eat, void, communicate etc.). The biological background is the concept of modes of behaviour exhibited within a circadian time scale [42].

The selection of representative modes of behaviour (in sum 35 modes) means action selection for the realization of a subjective intention or biological need,

feasible in an appropriate environment. If one or more modes of behaviour do not operate, or the operation of others persists, each pattern of the behavioural displacement may exert destructive effects such that the person develops a psychobiological disorder.

According to our clinical experience this questionnaire offers an element for the diagnostic assessment of an action-oriented classification of mental disorders and it also offers the basis for therapeutic actions by restitution of the capacity of the patient to act appropriately in everyday life. In addition, parameters for computer supported diagnostic and therapeutic programs can be clinically explored.

CONCLUDING REMARKS

Admittedly, representative clinical studies are necessary which enable a possible empirically based action-oriented classification of mental disorders. However, presently we can already apply this approach to therapeutic actions. As an example, we suppose that the so-called variants of normal life are basically caused by diverse stress-impairments of the function of synapses, such that these react with a decrease of the production of neurotransmitters or neuromodulators. In these disorders a low dosis of an antidepressant might be helpful in order to cope with this deficiency. Such a therapeutic “ex iuvantibus” procedure can biologically restitute the capacity of the patient to act appropriately in his/her everyday life. In addition, we suppose that many non-psychotic psychiatric patients may be “exhausted” in a broad sense. The action-oriented classification of mental disorders may improve psychiatric research and clinical practice in particular. Finally, it should be mentioned that the question as to how and where intentional programs are generated in the brain [43] is not the topic of this study.

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