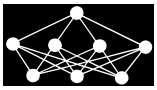

The Schizophrenic Brain: A Broken Hermeneutic Circle

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Abstract: A unifying picture to the hermeneutical approach to schizophrenia is given by combining the philosophical and the experimental/computational approaches. Computational models of associative learning and recall in the cortico-hippocampal system helps to understand the circuits of normal and pathological behavior.

Key words: *Schizophrenia, Hermeneutics, Computational Models, Associative Memory*

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1. Introduction

Hermeneutics is a branch of continental philosophy which treats the understanding and interpretation of texts. *Philosophical hermeneutics* emphasizes existential understanding instead of interpretation. *Critical hermeneutics* offers a methodologically self-reflective reconstruction of the social foundations of discourse and inter-subjective understanding. Finally, *phenomenological hermeneutics* is an attempt to synthesize the various hermeneutic currents. For an introduction for non-philosophers please refer to [1]. One of the most important concepts in hermeneutics is the hermeneutic circle. This notion means that the definition or understanding of something employs attributes which already presuppose a definition or understanding of that thing. The method is in strong opposition to the classical methods of science, which do not allow such circular explanations.

Motivated by Ichiro Tsuda [2, 3] who applied the principles of hermeneutics to the brain by using chaos as a mechanism of interpretation, one of us (PE)

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played with the idea [4] of how, if at all, two extreme approaches, the "device approach" and the "philosophical approach" could be reconciled. It was cautiously suggested by turning to the philosophical tradition that hermeneutics, i.e., the "art of interpretation", which is neither monist nor dualist a priori, can be applied to the brain. Further, we stated that the brain is both the "object" of interpretation as well as the interpreter: therefore the brain is itself a hermeneutic device. For our dialog with Tsuda see [5].

Recently new initiatives for applying hermeneutics in the context of neuroscience and cognitive science have emerged. Chris Firth [6] uses neural hermeneutics as the neural basis of social interaction, and explains psychiatric disorders, such as schizophrenia, as failure in the ability to interpret (represent and model) the world. Shaun Gallagher's analysis points out that hermeneutics and cognitive science have an overlapping interest [7].

Independently from our interest in hermeneutics we have started to work on combined behavioral, brain imaging and computational approaches to associative learning in healthy and schizophrenia patients to explain their normal and reduced performance. The working hypothesis we adopt is that schizophrenia is a "disconnection syndrome", as was suggested among others by Friston and Frith [8] and our aim is to qualitatively and quantitatively understand the functional bases of these disconnections.

Rethinking these studies from the perspective of the hermeneutic approach together with the preliminary results of our combined experimental and computational studies [9, 10] leads us to believe that the hermeneutic circle necessary to associative learning is broken in schizophrenic patients, and that therapeutic strategies should act to repair this circle.

In this paper we provide a unifying approach for combining the philosophical and experimental/computational approaches. First, we briefly review both our own old perspective and newer developments on neural hermeneutics (Sec. 2., Sec. 3.). Then we provide a sketch of the associative learning paradigm (Sec. 5.), specific neural implementations (Sec. 6.), and computational models of hippocampal associative learning and prefrontal - hippocampal interactions (Sec. 7.). Simulation results suggest that reduced performance of schizophrenia patients may be due to reduced cognitive capacity and learning rate related to impairment of functional connectivities between brain regions.

2. The brain as a hermeneutic device

The brain can be considered as a device of different types. Among these: a thermodynamic device, a control device, a computational device, an information storing, processing and creating device, or a self-organizing device.

The device approach is strongly related to the *dynamic metaphor* of the brain [11]. Dynamic systems theory offers a conceptual and mathematical framework to analyze spatiotemporal neural phenomena occurring at different levels of organization. These include oscillatory and chaotic activity both in single neurons and in (often synchronized) neural networks, the self-organizing development and plasticity of ordered neural structures, and learning and memory phenomena associated

with synaptic modification. Systems exhibiting high structural and dynamic complexity may be candidates of being thought of as hermeneutic devices. The human brain, which is structurally and dynamically complex thus qualifies as a hermeneutic device. One of the characteristic features of a hermeneutic device is that its operation is determined by circular causality. Circular causality was analyzed to establish self-organized neural patterns related to intentional behavior [20].

The world of systems determined by linear (and only linear) causal relationships belongs to the class of "simple systems" or mechanisms. The alternative is not a "subjective" world, immune to science, but a world of complex systems, i.e., one which contains closed causal loops.

Systems with feedback connections and connected loops can be understood based on the concepts of circular and network causality. Leaving aside the clear and well-organized world of linear causal domains characterizing "simple systems" we find ourselves in the jungle of the complex systems [21].

As we know from engineering control theory, large systems consist of both controller and controlled units. The controller discharges control signals towards the controlled system. The output of the controlled system is often sent back to the controller ("feedback control") forming a closed loop. Negative feedback control mechanisms serve to reduce the difference between the actual and the desired behavior of the system. In many cases, specific neural circuits implement feedback control loops which regulate specific functions.

Analyzing the question of whether the technical or "device approach" to the brain and the "philosophical approach" can be reconciled, it has been concluded that the brain is a physical structure which is controlled by, and also controls, learns and teaches, processes and creates information, recognizes and generates patterns, organizes its environment and is organized by it. It is an "object" of interpretation, but also it is itself an interpreter. The brain not only perceives but also creates new reality: it is a hermeneutic device [4].

3. Hermeneutics, cognitive science, schizophrenia

Frith's research group is working on establishing a scientific discipline they call neural hermeneutics dealing with the neural basis of social interaction. The key elements of their approach is the assumption that representations of the external world can be shared with others, and these shared representations may be the basis of predicting others actions during interactions. They use combined behavioral and brain imaging studies to uncover both the normal neural mechanisms, and pathological ones leading to schizophrenia.

Gallagher's analysis implies: (i) Hermeneutics and cognitive science is in agreement on a number of things. An example is the way we know objects. The interpretation of objects needs "schema theory" (a modern version is given by Michael Arbib [22]); (ii) Hermeneutics can contribute to cognitive science. The basis of the argument is that understanding situations needs hermeneutic interpretation. The usual critique is that logic, rule-based algorithms, and other similar computational methods are too rigid to interpret ill-defined situations, but hermeneutics "the art of interpretation" can do it. ("Mental models", which help to analyze situations also should have mentioned. Mental models have played a fundamental role in

thinking and reasoning, and were proposed in a revolutionary suggestion by Kenneth Craik (1914 - 1945) [23]. The idea that people rely on mental models can be traced back to Craik's suggestion that the mind constructs "small-scale models" of reality that it uses to predict events.); (iii) Cognitive science also has something to offer to hermeneutics, particularly to understand other minds. The most popular notion today is the *theory of mind* or more precisely "theory of other's minds". The most effective method of cognitive science to understand other minds, i.e. to show empathy is to simulate other minds by using analogical thinking [24]. The neural basis of theory of mind now seems to be related to mirror neurons, which is a key structure of imitation, and possibly language evolution [25]. A failure of attributing self-generated action generated by the patient himself (what we may label as the lack of ability to close the hermeneutic circle) can be characteristic for schizophrenia patients [26].

4. Nonlinear Dynamics and Schizophrenia

Dynamic system theory offers conceptual and mathematical tools for describing the performance of neural systems at very different levels of the organization [11].

It is generally accepted that schizophrenia is related to excessive pruning of cortical connections, and simple network studies [12] have shown that cortical pruning may lead to the formation of "pathological attractors".

Pathological attractors may implement the dynamic generation of positive symptoms in schizophrenia as these symptoms, including delusions and hallucinations can be activated in the absence of external cues. Related to the modifiability of the attractor-basin portrait, a model based on the NMDA receptor delayed maturation has also been suggested as a possible mechanism of the pathogenesis of schizophrenic psychotic symptoms [13].

Dynamical systems hypotheses are based on the assumption that pathological symptoms are related to changes in the geometry of the attractor basin portrait [14, 15]. A network model of excitatory and inhibitory neurons built by leaky integrate-and-fire models was used to design several simulation experiments to study the effects of changes in synaptic conductances on overall network performance. Reduction in synaptic conductances connected to glutamatergic NMDA receptors implied flatter attractor basins, and consequently less stable memory storage. Combined reduction of NMDA and GABA receptors imply such changes in the attractor structure, that may implement such positive symptoms, as hallucinations and delusion. More analyses are needed to relate impairment of global (interregional) and local (intraregional) connections to the emergence of schizophrenia. Nonlinear theories of schizophrenia have been suggested [16, 17] based on EEG recordings, but whereas EEG analysis is very extensively used, the theoretical bases remain unclear. On the one hand, classical signal analysis considers EEG records as the realization of (often stationary) stochastic processes, and spectral (and later also wavelet) analysis has been the conventional method to extract the dominant frequencies and other parameters of the rhythms. On the other hand, the occurrence of chaotic temporal patterns has been reported at different hierarchical levels of neural organization. Chaotic patterns can be generated at the single neuron level, due to the nonlinearity of voltage-dependent channel kinetics of the ionic

currents, at the multicellular network level, due to the interactions among neurons, and at the global level in consequence of spatiotemporal integration.

Dynamic systems theory offers a conceptual approach to EEG signal processing, different from the classical analysis. Time series, even irregular ones, are considered as deterministic phenomena generated by nonlinear differential equations. Though the methodological difficulties of interpreting the calculated quantities (Lyapunov exponents, fractal dimensions, entropies etc.) to characterize neurological categories are now well-known [18], the application of dynamic systems theory brought a breath of fresh air to the methodology of processing of neural signals. Schizophrenic symptoms may occur due to impairment in coupling of processes taking place at different temporal and spatial scale, and the structural basis of pathological changes in dynamics and behavior can be revealed by using dynamical models.

Recently extensive research has been employed to connect gamma rhythms to schizophrenia. While it is clear that there are region-specific changes in the gamma (and beta) rhythms, data for rodents and mammalians are controversial [19]. Working memory related to gamma rhythms is disrupted in schizophrenia patients. One reason for the changes in the gamma rhythm is related to modulation of the interaction between the glutamate and the NMDA receptors, and one possible pharmacological therapeutic procedure might be to use drugs acting on GABA receptors to reconstruct the rhythms.

5. Associative learning

Associative learning relies on the consolidation and retrieval of associations between diverse memoranda, sensory inputs and streams of neural activity, particularly by hippocampal and medial temporal lobe neurons. Our own studies have investigated the associative learning performance of healthy control and schizophrenia patients. Our employed learning procedure was not "one shot", but occurred over a series of encoding/consolidation and retrieval epochs: thus learning has an iterative characteristic. During the task subjects alternate between blocks of consolidation, rest/rehearsal and retrieval. During consolidation, nine equi-similiar objects with monosyllabic object names are presented in sequential random order (3s/object) in grid locations for naming (e.g. "bed" and "book"). Following a brief rest/rehearsal interval, memory for object-location associations is tested by cuing grid locations for retrieving objects associated with them (3s/cue). Object names are monosyllabic to minimize head motion. Eight blocks (each cycling between consolidation, rest and retrieval) are employed. Learning dynamics in controls and schizophrenia patients are shown on Figure 1.

6. Specific implementation of neural circular causality

There are several neural implementations of circular causality for our system. Three levels of connections - an anatomical, a functional and a neurochemical - will be mentioned.

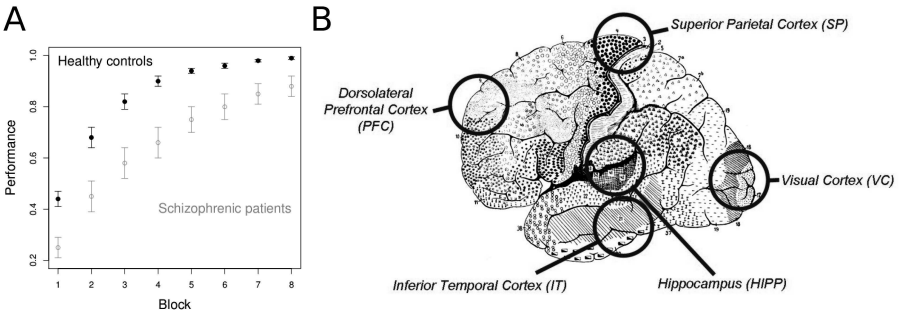

Fig. 1 *Learning dynamics and brain areas involved in the associative memory task. A: Learning dynamics in controls and schizophrenia patients over time are plotted. The data provide evidence of generally asymptotic learning in both groups, with reduced learning rates in patients compared to controls. B: Brain areas critically involved in the learning and recall of object-location pairs during associative memory task.*

6.1 Cortico-hippocampal loop

It is generally agreed that the hippocampal formation has a crucial role in learning and memory processes. The hippocampus is reciprocally connected to many neural centers and is thought to prepare information for long term storage. The cortico-hippocampal-cortex loop might be considered as the structural basis of a circular causal chain, where information can be stored, circulated, recalled and even created. Such kinds of loops have *control* functions.

6.2 The functional macro-network for object-location associative memory

fMRI data suggest that five interconnected regions (superior parietal cortex, inferiotemporal cortex, prefrontal cortex, primary visual cortex and the hippocampus) are involved to form a functional macro-network [27] (Fig. 1). In accordance with the spirit of the "disconnection syndrome" a question to be answered is: which connections are impaired during schizophrenia, and what is the measure of functional reduction of the information flow?

6.3 The glutamate - dopamine interplay

In addition to the macro-network, another type of loop (characterizing the neurochemical machinery) can be identified. The failure of this loop may also be related to schizophrenia. The dopamine hypothesis, which has been the predominant hypothesis, postulates that symptoms of schizophrenia may result from failure of the dopaminergic control system. Both increases (mostly in striatum), and decreases (mostly in prefrontal regions) in dopaminergic levels have been found. Glutamatergic mechanisms also seem to have a major role. Drugs that block neurotrans-

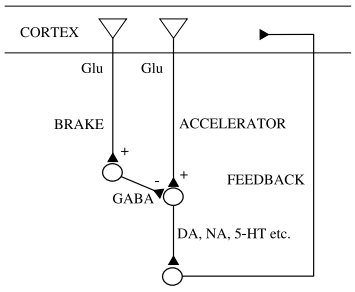

Fig. 2 *Hypothetical scheme showing the cortical regulation of the activity of the monoaminergic brainstem neurons by means of a direct glutamatergic pathway ("accelerator") and an indirect glutamatergic/GABAergic pathway ("brake"). Based on Fig. 1 of [29]. The impairment of the balance between "brake" and "accelerator" may explain both increase and decrease of dopamine level.*

mission at NMDA-type glutamate receptors cause symptoms similar to those of schizophrenia. The understanding of dopamine-glutamate interaction may lead to new therapeutic strategies [28]. A simple control loop for glutamatergic regulation of dopamine release [29] is illustrated on Fig. 2.

7. Computational Modeling

7.1 Modeling hippocampal associative learning

An earlier model [9] captured the dynamics of learning in healthy control and schizophrenia patients.

Subsequently, we have also developed a neural model incorporating brain regions involved in paired-associate learning in order to analyze the mechanisms underlying behavioural differences between schizophrenia and control subjects. The model has two parts: A simple visual system, and a more detailed model of the hippocampal formation [10] (Fig. 3).

We did not intend to model the visual signal processing system in its details, because these sensory areas are presumably not affected by the illness. The visual input consisted of 8x8 pixel sized, random images placed on a 16x16 pixel arena at 9 different, but overlapping positions. We built a simplified feed-forward network to analyze the retinal image, and to create the representations of the object (r_{it}, the model of the area IT in the ventral stream), and its location (r_{sp}, as the area SP in the dorsal stream) [10]. The proposed role of the hippocampus is to bind these two representation together [30] so that when cued by the location, the correct object can be recalled. The highly processed sensory input enters the hippocampus through the mossy fiber pathway, originating in the entorhinal cortex (which is not explicitly modeled here). The EC itself has reciprocal connections with both the hippocampus and various neocortical areas, including visual areas and is considered

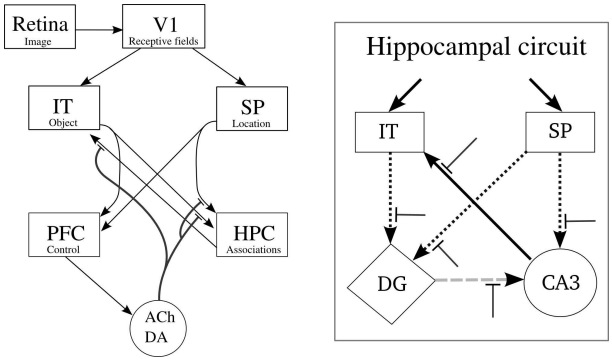

Fig. 3 *The architecture of the model. The retinal image is processed by neurons with simple receptive fields in the visual cortex (V1). The representation of the object and its location is generated in the inferior temporal cortex (IT) and the superior parietal cortex (SP), respectively. High level visual areas innervates both the hippocampus (HPC) and the prefrontal cortex (PFC). The hippocampus stores the associations, while the prefrontal cortex indirectly controls the process of learning and recall by modulating hippocampal synapses (grey T-arrows) via subcortical cholinergic (ACh) or dopaminergic (DA) areas. Right box: The details of the hippocampal region and its connections. DG: dentate gyrus, CA3: the CA3 region. Dotted: perforant path axons; dashed: mossy fibers.*

as a relay for information coming from multimodal association areas. Mossy fibers terminate on the dentate granule cells and hippocampal pyramidal neurons (Fig. 3, right). Two regions of the hippocampal formation were modeled: the dentate gyrus (DG) and the CA3 region. We used firing rate models, where the activation of each unit was calculated by the linear sum of its input.

7.2 The model architecture

Granule cells in the dentate gyrus receive information from both dorsal and ventral visual areas:

$$a^i_{dg} = \sum_j w^{ji}_{sp\to dg} r^j_{sp} + \sum_k w^{ki}_{it\to dg} r^k_{it}$$
$$r^i_{dg} = F(a_{dg}, sp_{dg}),$$

where a^i_{dg} is the activation of the i^{th} neuron in the dentate gyrus, r is the presynaptic firing rate and $w_{it\to dg}$ is the synaptic weight connecting neurons in the IT to neurons in the DG. $F()$ is a threshold linear function that transforms the activation into firing rate according to the sparseness of the representation, $sp_{dg} = \frac{\sum_i (r^i_{dg})^2}{N_{DG}(\sum_i r^i_{dg})^2}$.

Hippocampal pyramidal cells are innervated by granule cells as well as neocortical neurons:

$$a^i_{ca} = \beta \sum_j w^{ji}_{dg\to ca} r^j_{dg} + \gamma \sum_j w^{ji}_{sp\to ca} r^j_{sp}$$
$$r^i_{ca} = F(a_{ca}, sp_{ca})$$

Projection from the dentate gyrus to the hippocampus (called "mossy fibers", Fig. 3) determines the activity in the CA3 during learning ($\beta >> \gamma$), but is less effective during recall ($\gamma >> \beta$). The cortico-hippocampal loop is closed by the back-projection from the hippocampus to the neocortex:

$$a^i_{it} = \gamma \sum_j w^{ji}_{ca\to it} r^j_{ca}$$
$$r^i_{it} = F(a_{it}, sp_{it})$$

During *learning* synaptic connections in the IT, DG and CA3 were modified by simple Hebbian plasticity [31]:

$$\Delta w^{ij}_{sp\to dg} = \alpha r^j_{dg}(r^i_{sp} - w^{ij}_{sp\to dg})$$
$$\Delta w^{ij}_{it\to dg} = \alpha r^j_{dg}(r^i_{it} - w^{ij}_{it\to dg})$$
$$\Delta w^{ij}_{sp\to ca} = \alpha r^j_{ca}(r^i_{sp} - w^{ij}_{sp\to ca})$$
$$\Delta w^{ij}_{ca\to it} = \alpha r^j_{it}(r^i_{ca} - w^{ij}_{ca\to it})$$

Parameters r_{DG}, r_{CA3} and r_{IT} govern the amount of learning during a single episode in the corresponding areas. In this way, the hippocampal representations are associated to the representation of the original objects in the IT. During the *recall* connections are not modified. The attractor network in the IT helps the recall by converging to one of the learned objects.

We used moderate number of neurons in the simulations (typically 500 in one layer) in order to be able to implement distributed encoding in a realistic range of sparsity (0.1 in the hippocampus). Our hippocampal model was built according to the following key assumptions [32]:

- The DG performs pattern separation by competitive learning: it removes redundancies from the input and produces a sparse representation for learning in the CA3 region. This process can be considered as a translation from the neocortical to hippocampal language.
- The granule cells in the DG innervate CA3 pyramidal cells with particularly large and efficient synapses (the mossy fiber pathway) that makes postsynaptic neurons fire. Hebbian plasticity between active CA3 neurons and the perforant path axons associates the activity pattern in the CA3 to its incoming input (hetero-associative plasticity). After encoding, the same CA3 assembly can be activated by the presentation of the partial or noisy version of the original input (e.g., only the object or the location).

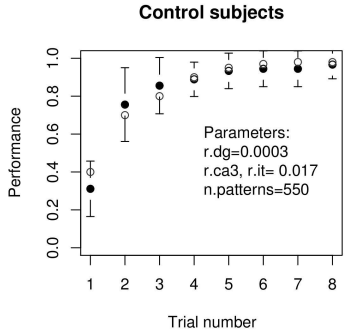

Fig. 4 *The performance of the model and comparison with the experimental data. Open circles: the same experimental data as on Fig. 1. Filled circles: performance of the model. Error bars show the standard deviation of ten independent trial.*

- Next, connections between CA3 cells and IT cells are modified, to translate the hippocampal to the neocortical code.

- Finally, objects are stored in a long term memory system in the inferior-temporal cortex forming an attractor network. During recall, the activity of this subsystem converges to one of the previously stored items (objects). The parameter $n_{patterns}$ is the number of objects stored in the IT.

The performance of the basic hippocampal model, quantified by the proportion of correctly recalled items, is shown on Figure 4. We note, that this is not the ideal performance of the model: The capacity of the system with 500 units and 0.1 sparsity is around a few hundreds of associations. However, with random initial synaptic weights and a small learning rate, it requires some repetitions to learn new associations appropriately.

7.3 Modeling fronto-hippocampal interactions

A newer version of the model was constructed by adding the prefrontal region which controls learning and recall processes presumably by modulating attention (Figure 3).

Modeling the prefrontal cortex. The prefrontal cortex plays a fundamental role in cognitive control, and in the coordination of thoughts and/or actions in relation to internal goals. The current model assumes that the prefrontal cortex (i) maintains task-related attention and (ii) depending on task conditions and input, prescribes the subtask to be executed. Generally speaking, in the context of the associative learning paradigm, the input structure and the assigned prefrontal control can be classified into two experimentally related demands: (i) Two inputs presented in conjunction must be bound and (ii) a location cue must lead to directed associative recall of its associated object. Reduced information flow between

parameter	control	patients	interpretation
n_{dg}	300		number of cells in the dentate gyrus
n_{ca3}	300		number of cells in the CA3 region
sp	0.1		sparseness of the hippocampal representation
r_{DG}	0.1		learning rate in the dentate gyrus
r_{CA3}	0.12		learning rate in the CA3
r_{IT}	0.1		learning rate in the IT
s_r	6.5 - 7	5.6 - 6	accuracy of the prefrontal control of plasticity
s_l	2		accuracy of the prefrontal control of synaptic efficacy

Tab. I *Parameter values used to generate control and schizophrenic behavior.*

prefrontal cortex and the hippocampus leads to impaired and noisy control leading eventually to poorer binding and reduced performance.

Controlled by the prefrontal cortex, the operation of the hippocampal network changes continually between the two extreme modes of operation: **learning** (encoding) and **recall** (retrieval). During learning modification of synaptic strengths is allowed, during recall synaptic strengths are fixed (see Fig. 5). During encoding activity of CA3 cells is determined by their mossy fiber (MF) input from the DG cells. Synaptic strengths of the perforant path (PP) – both in the DG and in the CA3 – are modifiable, while the strength of MF synapses do not change in time. During retrieval activity of CA3 cells is cued by its PP input. This subsystem operates as a hetero-associative network [32].

The prefrontal region is innervated by both the superior parietal and the inferior temporal areas. Based on the activation of these high level visual areas the PFC determines whether new association should be encoded within the hippocampal network (both the IT and the SP is active); or information should be recalled from the hippocampus (only one of them is active). Next, the prefrontal cortex sets (directly or indirectly via subcortical modulators such as ACh or Dopamine) the efficacy and the plasticity of the hippocampal synapses [33, 34]: Synapses marked by dotted line on the upper left panel of Figure 5 are active during learning, whereas other (complementer) pathways are mainly active during recall (upper right panel on Fig. 5); synapses marked by dashed line on the lower left panel of Figure 5 are plastic during learning.

7.4 Performance of the model

The performance of the hippocampal model on the associative learning task is shown in Figure 6. According to the model, the poorer performance on the associative learning task can be explained by less accurate control of learning and the recall processes. If the prefrontal cortex does not modulate learning and recall in hippocampal synapses, performance of the model will be poorer.

We would like to emphasize that a very small difference in prefrontal control can be responsible for less accurate performance in schizophrenia patients. The right panel of figure 6 shows the distribution of the parameters values controlled by the PFC for control (black) and patients (red). The two distributions are highly similar.

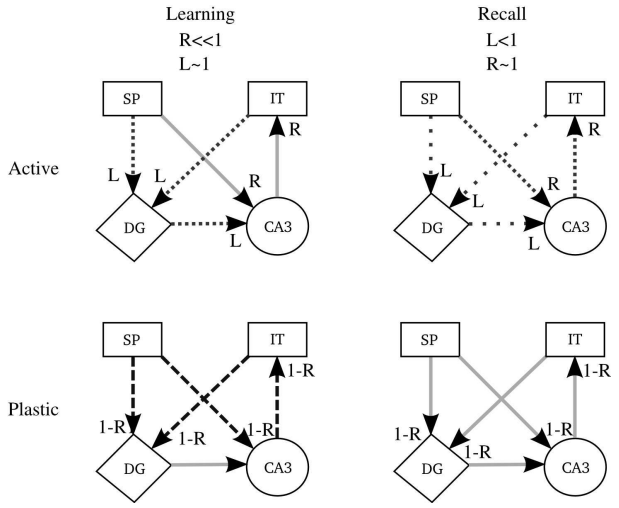

Fig. 5 *Modulation of hippocampal pathways by the prefrontal cortex. During learning (left column, L≈1 and R<<1) visual areas activates the dentate gyrus that excite CA3 pyramidal cells through mossy fiber synapses (dotted lines on upper left panel). The perforant path synapses and the hippocampal back-projections (dashed lines on the lower left panel) are modified by Hebbian plasticity rule. During recall (right column, L<1 and R≈1) the dentate gyrus is not activated, CA3 is activated through the direct pathway (perforant path), and CA3 recalls the learned object from the IT (upper right panel). None of the synapses are modified during recall (lower right panel).*

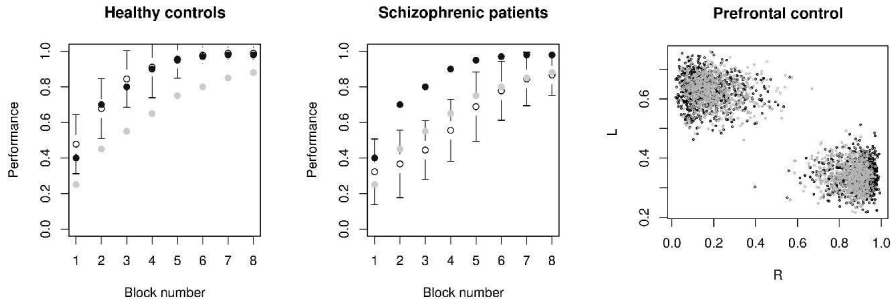

Fig. 6 *Learning curves for normal (left) and schizophrenic patients (middle). The only difference between the two models is that in the prefrontal control of the learning and recall process. Right: The distribution of the parameters R and L controlled by the prefrontal cortex in the normal (black) and the schizophrenic (grey case.*

8. Concluding remarks

The brain is considered as a hermeneutic device, which not only receives and processes incoming signals, but interprets them by some iterative mechanisms. In this paper we made an effort to integrate philosophical perspectives to the ones of experimental and computational neuroscience by demonstrating that at least some symptoms of schizophrenia may be understood as some failures in the hermeneutic circle. Control loops in chemical, network and regional levels might be the neural bases of the interpreting iterative mechanisms. Specifically, the impairment of cognitive control of the prefrontal cortex on hippocampal processes implies uncertainties in the task to be solved and will result in poorer performance in learning and recall processes.

While the breaking of the circle may lead to schizophrenic symptoms, combined pharmacological psychotherapeutic strategies should act to repair the circle.

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References

[1] Mallery J.C., Hurwitz R., Duffy G.,: Hermeneutics: From Textual Explication to Computer Understanding? In Shapiro, S.C. (ed.): The Encyclopedia of Artificial Intelligence John Wiley &Sons, New York (1987)

[2] Tsuda I.: A hermeneutic process of the brain. Prog. Theor. Phys. Suppl. 79, 241-259 (1984)

[3] Tsuda I.: Chaotic Itineracy as a Dynamical Basis of Hermeneutics in Brain and Mind. World Futures, 32, 167-184, (1991)

[4] Érdi P.: The brain as a hermeneutic device. BioSystems 38, 179-189 (1996)

[5] Érdi P., Tsuda I.: Hermeneutic approach to the brain: process versus device? Theoria et Historia Scientiarum VI, 307-321 (2002)

[6] Frith C.: Making Up the Mind: How the Brain Creates Our Mental World. Blackwell Publ. (2007)

[7] Gallagher S.: Hermeneutics and the Cognitive Sciences. J. of Consciousness Studies 10-11, 162-174 (2004)

[8] Friston K.J., Frith C.D.: Schizophrenia: A disconnection syndrome? Clin. Neurosci. 3, 88-97 (1995)

[9] Diwadkar V.A., Flaugher B., Jones T., Zalányi L., Ujfalussy B., Keshavan M.S., Érdi P.: Impaired associative learning in schizophrenia: Behavioral and computational studies. Cognitive Neurodynamics 2, 207-219 (2008)

[10] Érdi P., Ujfalussy B., Zalányi L., Diwadkar D.A.: Computational approach to schizophrenia: Disconnection syndrome and dynamical pharmacology. In: A selection of papers of The BIOCOMP 2007 International Conference L. M. Ricciardi (ed.) Proceedings of the American Institute of Physics 1028, 65-87 (2007)

[11] Érdi P.: On the 'Dynamic Brain' Metaphor. Brain and Mind 1,119-145, (2000)

[12] Hoffman R.E., McGlashan T.H.: Neural network models of schizophrenia. Neuroscientist 7, 441-54 (2001)

[13] Ruppin E.: NMDA receptor delayed maturation and schizophrenia. Medical Hypotheses 54, 693-697 (2000)

[14] Loh M., Rolls E.T., Deco G.: A Dynamical Systems Hypothesis of Schizophrenia. PLoS Comput Biol. 3, 2255-2265 (2007)

[15] Rolls E.T., Loh M., Deco G., Winterer G.: Computational models of schizophrenia and dopamine modulation in the prefrontal cortex. Nature Reviews Neuroscience, 9: 696-709 (2008)

[16] Bressler S.L.: Cortical Coordination Dynamics and the Disorganization Syndrome in Schizophrenia. Neuropsychopharmacology 28, S35-S39 (2003)

[17] Breakspear M.: The nonlinear theory of schizophrenia. Australian and New Zeeland J. Psychiatry 40, 20-35 (2006).

[18] Palus M.: Nonlinear dynamics in the EEG analysis: Disappointments and perspectives. In Rapp P.E., Pradhan N., Sreenivasan R. (eds.): Nonlinear Dynamics and Brain Functioning, Nova Science Publishers (1999)

[19] Roopun A.K., Cunningham M.O., Racca C., Alter K., Traub R.D., Whittington M.A.: Region-specific changes in gamma and beta2 rhythms in NMDA receptor dysfunction models of schizophrenia. Schizophr Bull. 34, 962-973 (2008)

[20] Freeman W.J.: Consciousness, Intentionality, and Causality. Journal of Consciousness Studies. 6, 143-172 (1999)

[21] Érdi P.: Complexity Explained. Springer Publ. (2007)

[22] Arbib M.A., Érdi P., Szentágothai J.: Neural Organization: Structure, Function, Dynamics. The MIT Press, Cambridge, MA (1997)

[23] Craik K.: The Nature of Explanation. Cambridge Univ. Press. (1943)

[24] Barnes A., Thagard P.: Empathy and analogy. Dialogue: Canadian Philosophical Review 36, 705-720 (1997)

[25] Arbib M.A.: The mirror system, imitation, and the evolution of language. In: Nehaniv C., Dautenhahn K. (eds.): Imitation in Animals and Artefacts. MIT Press, Cambridge, MA 229-280 (2002)

[26] Arbib M.A., Mundhenk T.N.: Schizophrenia and the Mirror System: An Essay, Neuropsychologia 43, 268-280 (2005)

[27] Lavenex P., Amaral D.G.: Hippocampal-neocortical interaction: A hierarchy of associativity. Hippocampus 10, 420-430 (2000)

[28] Javitt D.C.: Glutamate and Schizophrenia: Phencyclidine, N-Methyl-d-Aspartate Receptors, and Dopamine-Glutamate Interactions. Int Rev Neurobiol. 78, 69-108 (2007)

[29] Carlsson A., Waters N., Waters S., Carlsson M.L.: Network interactions in schizophrenia - therapeutic implications. Brain Research Reviews 31, 342-349 (2000)

[30] Milner B., Johnsrude I., Crane J.: Right medial temporal-lobe contribution to object-location memory. Philos Trans R Soc Lond B Biol Sci. 352(1360), 1469-74 (1997)

[31] Gerstner W., Kistler W.M.: Spiking Neuron Models. Cambridge University Press (2002)

[32] Rolls E.T., Treves A.: Neural Networks and Brain Function. Oxford University press (1998)

[33] Hasselmo, M.E.: The role of acetylcholine in learning and memory. Curr. Opinion Neurobiol. 16(6), 710-715 (2006)

[34] Yao W.D., Spealman R.D., and Zhang J.: Dopaminergic signaling in dendritic spines. Biochem Pharmacol. 75(11): 2055–69 (2008)