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Nature and main kinds of psychopathological mechanisms

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The paper deals with two central issues in the philosophy of neuroscience and psychiatry, namely those of the nature and the major kinds and types of psychopathological mechanisms. Contrary to a widespread view, I argue that mechanisms are not kinds of systems but kinds of processes unfolding in systems or between systems. More precisely, I argue that psychopathological mechanisms are sets of actions and interactions between brain-systems or circuits as well as between the latter and other systems in one's body and external environment, both physical and social, involved in human psychopathology. According to the kinds of properties of the interacting systems or their component-parts, psychopathological mechanisms may be physical, chemical, biological, psychological, social, or, typically, mixed ones. Furthermore, I focus on two main kinds of psychopathological mechanisms involved in the causation of mental disorders, namely the pathogenetic and pathophysiological ones, stressing the importance of their careful distinction for the integrative understanding of otherwise disparate and apparently incommensurable psychiatric research findings. I illustrate my analysis with an example drawn from contemporary research on the mechanisms of acute psychosis. Finally, I stress the relevance of psychopathological mechanisms to a more scientifically-grounded classification of mental disorders.

Keywords: mechanisms, explanation, psychopathology, pathogenesis, pathophysiology, mental disorders, classification

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INTRODUCTION

The issues of the nature of mechanisms and their relevance to scientific research and understanding are at the center stage of contemporary philosophy of science and neuroscience (Glennan, 1996, 2002; Machamer et al., 2000; Bunge, 2003, 2006; Psillos, 2004; Craver, 2007; Bechtel, 2008). Recently, these topics have attracted the attention of both psychiatrists interested in the philosophy of psychiatry and philosophers of science interested in psychiatry (Kendler, 2008; Kendler and Parnas, 2008). Among the several motivations underlying this recent revival of interest in mechanisms and their relevance to psychiatry, one should note the following two major ones: First, the widespread recognition of the fundamental role the discovery of mechanisms plays in genuine scientific explanations, psychopathological ones included, and, second, the growing dissatisfaction with the scientific shortcomings of current psychiatric taxonomy, especially with the poor validity of many of its constituent categories as defined by exclusively clinical-descriptive features (Sirgiovanni 2009a, 2009b; van der Stel, 2009). True, many speculative and simplistic attempts were made in the past to provide mechanism-based global accounts of mental disorders, from the demonic possession paradigm in the Middle-Ages - through that of the libidinal fixation and regression to immature psychosexual stages in Freudian psychoanalysis- to the fashionable new-age past-trauma ones in the recent past (Lilienfeld et al., 2003). By contrast, the spectacular contemporary progresses in clinical and social neuroscience, as well as in social and psychiatric epidemiology, jointly with the rise and consolidation of the scientific evidence-based approach to all aspects of human psychopathology, including its causal mechanisms, render such a new attempt more scientifically promising, providing safeguards against the speculative excesses of the past. However, the fruitfulness of this enterprise presupposes- among other assumptions of a philosophical nature- a more clear understanding of the core

concept of mechanism as well as of the kinds and types of psychopathological mechanisms. In this paper, I will try precisely to deal succinctly with both these issues, stressing their crucial relevance for a more scientifically-grounded classification of mental disorders.

ON MECHANISMS AND MECHANISM-BASED EXPLANATIONS

One mainstream contemporary view holds that a mechanism is "a complex system that produces its behavior by the interaction of a number of parts according to direct causal laws" (Glennan, 1996, 2002). The main problem with this view is that it fails to draw a clear distinction between the complex system as a whole and its mechanisms, i.e. the interactions among its parts, the latter explaining why the former, as a whole, behaves as it does. In other words, mechanisms are always mechanisms of a system's of some kind specific behavior or, better, of its specific function(s), but they are not themselves systems. In fact, they are sets of actions of and/or interactions between a system's component-parts, as we will see in a moment.

According to another very influential view, known as "pluralist" view, "mechanisms are entities and activities organized in such a manner that they are productive of regular changes from start or set-up to finish or termination conditions" (Machamer et al., 2000).The major problem with this view is that the actions and interactions in question ("activities") are considered, at least in principle, as being distinct and independent from the "entities" which perform them. In other words, both entities and activities are thought to exist in principle on a par, which is why this definition of the concept of mechanism requires a third clause, namely that of their mutual organization in the previously specified manner. Precisely this parity between activities and entities accounts for the "pluralism" of this view. However, it seems difficult to admit the autonomous existence of activities detached from the entities which carry them out. More generally, activities as processes are regular continuous changes of a concrete entity's properties and thus, far from being autonomous, they depend essentially upon the latter (Bunge, 1977; Psillos, 2004). Moreover, this view also conflates the concept of a system with that of its mechanism(s). Finally, the reference to start and finish conditions seems misleading, since mechanisms involve ongoing feed-back processes rather than unidirectional changes (Thagard, 2006). Owing to the preceding deficiencies of these explications of the concept of mechanism, I will adopt in the following another elucidation of this concept, according to which, "mechanisms are sets of processes in a system (i.e. among its component parts and/or among the latter and other systems in its immediate external environment), such that they bring about or prevent some change in the system as a whole" (Bunge 2003, p.20). This view avoids the shortcomings of the previous ones and, moreover, it is broad enough to encompass the rich variety of kinds of mechanisms relevant to the scientific understanding, prevention and treatment of human psychopathology. The overall mechanism-based approach to human psychopathology can be sketched thus: One begins from an initial and provisional description of a relevant molar mental function (dysfunction) carried out by the whole human brain in specified conditions. Then, one proceeds to the anatomical and functional decomposition of the latter in search of the localization of the brain sub-systems and their mutual interactions which carry out the molar mental function (dysfunction) in question. In the process, one obtains a more accurate identification of the initial mental function (dysfunction) which, in turn, enables the more accurate localization of the systems carrying it out in the course of the "virtuous" circle of scientific research. At each level of organization, the mechanisms of the specific functions (dysfunctions) of some brain sub-system or circuit are explained by the specific actions and interactions of its component parts. However, all brain systems interact with other systems as well, both internal and external to the individual organism (other brain systems, remaining organ systems, as well as systems in individual organisms' physical and above all social environments respectively), and are thus equally affected by them in carrying out their specific functions. Accordingly, their optimal scientific investigation should integrate the "top-down" with the "bottom-up" approaches in

inter-level hypotheses and theories spanning all relevant levels of organization. To this end, hypotheses and theories at different levels should co-evolve by mutual adjustments and corrections in order to maximize the overall scientific validity of the resultant integrated theory.

PSYCHOPATHOLOGICAL MECHANISMS

Kinds and Types of Psychopathological Mechanisms

In the case of human psychopathology, psychopathological mechanisms are kinds of processes in and between concrete systems involved in the causation, clinical expression and experiential content, maintenance or perpetuation, protection or prevention and, finally, amelioration or cure of mental disorders. The concrete systems in question are the brain, the remaining body systems, and the systems in one's physical and above all social environment. Accordingly, all the preceding kinds of psychopathological mechanisms are sets of actions of and interactions between human brain's subsystems or circuits as well as between the latter and other systems in one's body and external environment, both physical and social. From this point of view, psychopathological mechanisms do not differ from normal psychological mechanisms. Their difference lies in that whereas normal psychology focuses on the mechanisms underlying the performance of normal mental functions, psychopathology focuses on those determining mental dysfunctions or malfunctions and the patterns thereof. Of note, most clinical disturbances of human mental functions, such as thought, affect or perception, are still only coarsely delineated in contemporary descriptive psychopathology (see e.g. Oyebode, 2008). Accordingly, they are in need of further refinement in order to facilitate the scientific investigation of their mechanisms, following the example of contemporary memory research (Squire and Kandel, 1999, van der Stel, 2009). In turn, any improvement in the scientific understanding of their underlying mechanisms would enable their more accurate clinical delineation. Overall, our descriptive knowledge of the clinical disturbances of human mental functions co-evolves with our understanding of their mechanisms by continuous mutual adjustments, constraints and corrections.

Moreover, each of these kinds of psychopathological mechanisms comes in various types, according to the kinds of properties possessed by the interacting systems or their component-parts (sub-systems). Thus, psychopathological mechanisms may be physical, chemical, biological, psychological, social, or, more typically, mixed ones, associating to the final psychological or mental component of the overall mechanism several components of the remaining types. Some simple but uncontroversial examples: The main mechanism of mental disorders due to general medical conditions is presumably the direct action on human CNS of disease processes in other body systems (bio-psychological). Moreover, in adjustment disorders the main mechanism is presumably the action on human CNS of strongly adverse psycho-social life-events (interpersonal- or socio-psychological). However, typically, the mechanisms involved in mental disorders are integrated in complex networks of synergistically interacting systems of several types in the form of positive feed-back or feed-forward loops (for a judicious example of such networks in the case of alcoholism, see Kendler, 2008). Furthermore, some mechanisms may be temporally distal or primary in their activation, whereas others temporally proximal or secondary ones, i.e. their activation is conditional upon the temporally prior activation of the distal or primary ones. Core examples: Pathogenetic and pathophysiological mechanisms respectively (see below). In addition, some mechanisms- whether temporally primary or secondary- may be necessary, essential or core-mechanisms, in the sense that they are invariably involved in the causation, clinical expression and experiential content, maintenance, protection and prevention or finally, the amelioration or cure of mental disorders, whereas others accessory, auxiliary or peripheral only ones, in the sense that though they are not necessary, jointly with the core-mechanisms are sufficient for the occurrence of the outcome of interest in the given respect. For instance, according to the prevalent generic model for most mental disorders, namely the vulnerability-stress model, the stressful events might be quite non-specific or even trivial. However, jointly with the more spe-

cific traits of patients' underlying strong vulnerability, they can be sufficient enough to trigger the pathophysiological mechanisms of the mental disorder. Thus, the mechanisms of patients' exposure to these stressful events could be only peripheral, by contrast to those underlying their vulnerability which could be central ones. However, the reverse may also obtain, whereby a strong psycho-social stress load- even on a background of weak pre-morbid vulnerability- can result in the clinical manifestations of a mental disorder. Here, the psycho-social mechanisms should be considered as necessary and thus central ones. This might the case, for example, in several cases of anxiety and mood disorders, as attested by robust research findings from the fields of social epidemiology and psychiatry (e.g. Dohrenwend, 1998). Finally, some mechanisms may be pro-active in their operation, while others reactive ones, activated in order to counteract, neutralize or compensate for the operation of the former. For example, according to Eugen Bleuler, the pathophysiological mechanisms of secondary symptoms in schizophrenias such as delusions, autism and negativism, were hypothesized by him to be compensatory or reactive to the activation of those involved in the generation of primary schizophrenic symptoms such as loosening of associations and psychomotor disturbances (Bleuler, 1911).

At any rate, the final effects of all types of psychopathological mechanisms are necessarily mediated by individuals' minding brains through their impact on them. Thus, brain systems carrying out mental functions are the central or ultimate referents of psychopathological explanations, though not necessarily the more weighty ones .

In the present paper, I shall focus on the mechanisms involved in the causation of mental disorders, leaving aside several other important kinds of psychopathological mechanisms such as psycho-protective, psycho-pathoplastic- shaping the experiential content and clinical expression of patients' symptoms- and psycho-patholytic ones, underlying patients' recovery, whether spontaneously or under biological or psychological therapeutic interventions.

Pathogenetic and Pathophysiological Mechanisms

With respect to the causation of mental disorders, one should carefully distinguish -though not separate or detach- the pathogenetic mechanisms from the pathophysiological ones. The activation and operation of the pathogenetic mechanisms determines the development of the initial increased vulnerability to mental disorders. By contrast, the activation of the pathophysiological mechanisms- on the grounds of a previously developed increased vulnerability or, alternatively, of an increased concurrent psycho-social stress load- leads to the emergence of the clinical manifestations of their respective clinical syndromes. Jointly, the pathogenetic and pathophysiological mechanisms could provide the essentials of the causal history of some category of mental disorder. Pathogenetic mechanisms are temporally distal or primary, by contrast to pathophysiological mechanisms which are temporally proximal and thus secondary. This distinction becomes problematic only in cases of acute mental disorders, such as e.g. substance intoxication or delirium. In general, one could plausibly presume that the proximal and contiguous to patients' clinical psychopathology pathophysiological mechanisms will prove more robust than their more distal pathogenetic ones. Both sets of mechanisms may contain necessary and auxiliary members. Likewise, both sets of mechanisms are likely to contain both pro-active and reactive ones. Finally, both sets of mechanisms can presumably combine mechanisms of several types.

If the conceptual distinction between pathogenetic and pathophysiological mechanisms of human psychopathology were not always carefully respected, which is unfortunately often the case, serious misunderstandings might arise in the interpretation of the relevance and scope of psychiatric research findings for our causal understanding of mental disorders. In the preceding, I assumed tacitly the validity of the vulnerability-stress or more generally of a "double-hit" generic model for the whole of mental disorders. However, this distinction holds for the whole of medicine, even in cases whereby a single con-

tinuous disease-process leads, once activated, invariably to its clinical manifestations: "Pathophysiology differs from pathogenesis. Pathogenesis is the mode of origin or development of any disease process (e.g. development of autoimmunity to the thyroid-stimulating hormone receptor). Pathophysiology describes the resulting disordered physiology and clinical consequences (release of excess thyroid hormone, producing the syndrome of hyperthyroidism" (Mc Phee et al., 1995, p.1).

The paramount importance of the discovery and understanding of psychopathological mechanisms, especially of those involved in the causation of mental disorders, for the consolidation of the scientific foundations of psychiatry, cannot be overestimated. Several recent authors have stressed the rather severe shortcomings of the descriptivist turn of psychiatric taxonomy during the last three decades, inaugurated by the publication of DSM-III and consolidated in its subsequent revisions (American Psychiatric Association, 1980, 1987, 1994, 2000). These shortcomings or even anomalies- since they seem unexplainable within the strictly clinical descriptive DSM framework- include the excessive clinical heterogeneity of patients subsumed under the same diagnostic category, mental patients' well above chance diagnostic "co-morbidities" and the poor overall validity of most of its constituent diagnostic categories, to name but a few (see e.g. Aragona, 2006, 2009; Murphy, 2006; Oulis, 2008; Sirgiovanni, 2009a, 2009b). By "validity" I mean the extent or degree to which a psychodiagnostic category represents accurately a class of patients sharing a sufficiently stable cluster of, directly and/or only indirectly, observable objective features. Moreover, the whole cluster of these features should discriminate qualitatively each diagnostic class from the remaining ones in at least one respect. On the face of the preceding shortcomings of current psychiatric diagnostic schemes, several authors defend the at least provisional shift of research focus from the validity to the clinical utility of psychiatric diagnosis (Kendell and Jablensky, 2003; Rodrigues and Banzato, 2009). By contrast, others recommend the search for causal mechanisms and their explicit incorporation as essential ingredients in any future scientific taxonomy of human psychopathology (e.g. Charney et al., 2002; Murphy, 2006; Kendler, 2008; Kendler and Parnas, 2008; Sirgiovanni, 2009a, 2009b; van der Stel, 2009).

Schizophrenic Disorders as an Example

In the following, I will provide a deliberately simplified example of psychopathological mechanism drawn from contemporary research findings on the pathophysiology of delusion-formation in acute psychosis (Howes and Kapur, 2009). Several and numerous causal factors- exerting their action through only partly understood pathogenetic mechanisms, underlie individuals' vulnerability to acute psychosis. These factors- physical, biological, psychological, social, or mixed ones- include genes, obstetric complications, urban birth and upbringing in extreme poverty, migrant status, chronic cannabis use, social isolation and lack of support. Their common final effect, grounding individuals' increased psychological vulnerability to acute psychosis, is presumed to consist in a sensitization of individuals' striatum (Broome et al., 2005). This endogenous or exogenous previous sensitization of acute psychosis-prone individuals' striatum is expressed by a strong propensity to increased pre-synaptic dopamine elevation and release in striatal regions of their brains. Moreover, these pre-synaptic dopamine elevation and release are psychologically experienced by patients as increased salience or subjective significance assigned to normally innocuous external or internal stimuli, or rather to their perceptual representations of the latter. In turn, these striatal regions activate cortical association areas which perform the psychological function of thinking-via their strong anatomical connections to them-activate cortical association areas via their strong anatomical connections to them, cortical association areas which perform the psychological function of thinking. By the same token, patients undergo the psychological process of explanation-seeking for their abnormal perceptual experiences, a process eventually culminating in delusion-formation.

Of note, the previous example of pathophysiological mechanism illustrates well the con-

strual of the generic concept of mechanism adopted here, namely as sets of processes between a system's constituent parts as well as between the latter and other systems in its environment. Moreover, the previous example shows that mental functions, suitably construed as functions of complex brain systems can retain their causal efficacy and thus their genuine explanatory role of both normal and abnormal human behavior. Thus, the systemic version of the mind-body identity thesis can defuse the usual charges against the latter, namely that it leads inexorably either to the causal inertness of the mental (materialist epiphenomenalism) or its radical elimination (eliminative materialism).

Psychopathological Mechanisms and Psychiatric Classification

Delineating the several different kinds of psychopathological mechanisms involved in mental disorders, especially in their causation, without conflating them is of enormous importance for the consolidation of the scientific basis of psychiatry. Future progress on this front is expected to have a tremendous impact not only to the quality of the scientific explanation and rational treatment of mental disorders, but on their very classification and diagnostic identification as well. Moving from the mere clinical patterns of their current identification both downwards and upwards by disclosing and incorporating psychobiological and psychosocial mechanistic patterns respectively in their identification, seems the best research strategy for the eventual and much hoped for advent of a scientifically valid taxonomy of human psychopathology. At present, it is widely acknowledged that besides their clinical heterogeneity- owing to the logically disjunctive nature of current diagnostic criteria- psychiatric syndromes are also highly heterogeneous with respect to their pathophysiological and a fortiori their pathogenetic mechanisms as well. The discovery and incorporation in their classification of distinct central pathophysiological mechanisms leading to otherwise similar clinical syndromes would then allow their diagnostic identification as distinct clinical-pathophysiological syndromes. Moreover, the discovery of their distinct pathophysiological mechanisms would in turn enable the more refined and accurate re-description of their initially unitary and undifferentiated clinical syndrome. Finally, the further discovery and incorporation of distinct pathogenetic mechanisms would allow the -fallible though perfectible- identification of genuine psychopathological kinds, grounded on the whole cluster of their pathogenetic, pathophysiological and clinical patterns (Oulis, 2008). The greater proximity of pathophysiological psychopathological mechanisms to their respective clinical syndromes- in comparison to that of their pathogenetic counterparts- makes their discovery and delineation the primary and more decisive, though of course not the sole, target of psychiatric nosological research. This contrasts with the frequent research attempts to ground psychiatric nosology almost exclusively to distal genetic or epigenetic factors (e.g. Craddock and Owen, 2005; Crow, 2008, respectively). Moreover, weighing all types of proximal mechanisms- by taking also into account the psycho-social ones- might enable the evidence-based refined diagnostic differentiation of several nowadays unitary clinical syndromes in distinct predominantly psycho-biological (formerly known as "endogenous") and psycho-social ("reactive") sub-types. Perhaps, a still missing chapter of DSM should be entitled "mental disorders due to severe psycho-social conditions".

CONCLUSIONS

In conclusion, the recent resurgence of interest in the topic of psychopathological mechanisms jointly with their potential to revolutionize all fields of psychiatric knowledge and expertise, psychiatric taxonomy and therapeutics included, raises the issue of their precise elucidation and systematization. Parts of this challenge were precisely the two topics touched upon at some length in this paper, namely those of the nature and the major kinds of psychopathological mechanisms along with their relevance to the classification of mental disorders, at a time of severe theoretical crisis of extant psychiatric taxonomies.

REFERENCES

American Psychiatric Association. Diagnostic and statistical manual of mental disorders, third edition (DSM-III). American Psychiatric Association, Washington DC, 1980.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders, third edition revised (DSM-III-R). American Psychiatric Association, Washington DC, 1987.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV). American Psychiatric Association, Washington DC, 1994.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR). American Psychiatric Association, Washington DC, 2000.

Aragona M. Aspettando la rivoluzione. Oltre il DSM-V: le nuove idee sulla diagnosi tra filosofia della scienza e psicopatologia. Editori Riuniti, Roma, 2006.

Aragona M. The role of comorbidity in the crisis of the current psychiatric classification system. Philos Psychiatr Psychol 2009;16:1-11.

Bechtel W. Mental mechanisms: Philosophical perspectives on cognitive neuroscience. Routledge, New York, 2008.

Bleuler E. Dementia praecox oder Gruppe der Schizophrenien. Franz Deuticke, Leipzig und Wien, 1911.

Broome MR, Woolley JB, Tabraham P, Johns LC, Bramon E, Murray GK, Pariante C, McGuire PK, Murray RM. What causes the onset of psychosis? Schizophr Res 2005;79:23-34.

Bunge M. The furniture of the world. Reidel, Dordrecht, 1977.

Bunge M. Emergence and convergence: Qualitative novelty and the unity of knowledge. University of Toronto Press, Toronto, 2003.

Bunge M. Chasing reality: Strife over realism. University of Toronto Press, Toronto, 2006.

Charney DS, Barlow DH, Botteron K, Cohen JD, Goldman D, Gur R, Lin KM, Lopez JF, Meador-Woodruff JH, Moldin SO, Nestler EJ, Watson SJ, Zalcman SG. Neuroscience research agenda to guide development of a pathophysiogically based classification system. In: Kupfer DJ, First MB, Regier DA. (Eds) A research agenda for DSM-V. American Psychiatric Association, Washington DC, 2002:31-83.

Craddock NJ, Owen MJ. The beginning of the end for the Kraepelian dichotomy. Br J Psychiatry 2005;186:364-366.

Craver C. Explaining the brain: Mechanisms and the mosaic unity of neuroscience. Oxford University Press, New York, 2007.

Crow TJ. Craddock & Owen vs Kraepelin: 85 years late, mesmerized by "polygenes". Schizophr Res 2008;103:156-160.

Dohrenwend BP. Adversity, stress and psychopathology. Oxford University Press, New York, 1998.

Glennan S. Mechanisms and the nature of causation. Erkenntnis 1996;44:50- 71.

Glennan S. Rethinking mechanistic explanation. Philos Sci 2002;69:S342- S353.

Howes OD, Kapur S. The dopamine hypothesis of schizophrenia: Version III-The final common pathway. Schizophr Bull 2009;35:549- 562.

Kendell R, Jablensky A. Distinguishing between the validity and utility of psychiatric diagnoses. Am J Psychiatry 2003;160:4- 12.

Kendler KS. Explanatory models for mental illness. Am J Psychiatry 2008;165:695- 702.

Kendler KS, Parnas J. (Eds) Philosophical issues in psychiatry: Explanation, phenomenology, and nosology. Johns Hopkins University Press, Baltimore, 2008.

Lilienfeld SO, Lynn SJ, Lohr JM. (Eds) Science and pseudoscience in clinical psychology. Guilford Press, New York, 2003.

Machamer P, Darden L, Craver C. Thinking about mechanisms. Philos Sci 2000;67:1-25.

McPhee SJ, Lingappa VR, Ganong WF, Lange JD. (Eds) Pathophysiology of disease: An introduction to clinical medicine. Appleton and Lange, East Norwalk Connecticut, 1995.

Murphy D. Psychiatry in the scientific image. MIT Press, Cambridge Massachusetts, 2006.

Oulis P. Ontological assumptions of psychiatric taxonomy: main rival positions and their critical assessment. Psychopathology 2008;41:135-140.

Oyebode F. Sims' symptoms in the mind: An introduction to descriptive psychopathology. Saunders, Philadelphia, 2008.

Psillos S. A glimpse of the secret connection: Harmonizing mechanisms with counterfactuals. Perspect Sci 2004;12:288- 319.

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Rodrigues ACT, Banzato CEM. A logical-pragmatic perspective on validity. Dial Phil Ment Neuro Sci 2009;2:40-44.

Sirgiovanni E. Verso una tassonomia psichiatrica alternativa: La classificazione dei disturbi mentali da una prospettiva cognitiva della mente. PhD Thesis, University of Siena, June 2009a.

Sirgiovanni E. The mechanistic approach to psychiatric classification. Dial Phil Ment Neuro Sci 2009b;2:45-49.

Squire L, Kandel E. Memory: From molecules to man. Freeman, New York, 1999.

Thagard P. Hot thought: Mechanisms and applications of emotional cognition. MIT Press, Cambridge Massachusetts, 2006.

Van der Stel. Psychopathologie: Grondslagen, determinanten, mechanismen. Uitgeverij Boom, Amsterdam, 2009.