Journal of Health Sciences (J Health Sci) 2012; (2)4:39–47
Open Access
Open Journal Systems of Radom University in Radom, Poland ISSN 1429-9623 / 2012

COMPUTATIONAL APPROACH TO NEURAL PLASTICITY OF NERVOUS SYSTEM ON SYSTEM LEVEL

Podejście obliczeniowe do neuroplastyczności układu nerwowego na poziomie systemowym

Emilia Mikolajewska[1], Dariusz Mikolajewski[2]

[1]Rehabilitation Clinic, The 10th Clinical Military Hospital with Policlinic, Bydgoszcz, Poland
[2]Department of Informatics, Nicolas Copernicus University, Torun, Poland

Keywords: neurorehabilitation; physiotherapy; neural plasticity; cortical plasticity.

Abstract

Neuroplasticity (brain plasticity, cortical plasticity) is perceived an ability of nervous system to be changed (both in functional and structural areas) by processed signals (i. e. through activity, changes in environment, etc.).

Better understanding of the mechanisms underlying neuroplasticity on the system level may benefit newest therapy strategies designed to more effectively promote recovery of function. It can help guide and focus research and clinical practice to greater efficacy and better functional outcomes in neurorehabilitation and increased patients quality of life.

Computational models of processes associated with neuroplasticity on system level may be especially useful for deriving possible neuroplasticity mechanisms. This article aims at investigating the extent to which the available opportunities are being exploited, including own concepts, research and observations.

Słowa kluczowe: rehabilitacja neurologiczna; fizjoterapia; neuroplastyczność.

Streszczenie

Neuroplastyczność stanowi zdolność układu nerwowego do zmian (zarówno w zakresie funkcjonalnym, jak i strukturalnym) w wyniku oddziaływania przetwarzanych sygnałów (wynikających z działania, zmian w otoczeniu i innych).

Lepsze zrozumienie mechanizmów leżących u podstaw neuroplastyczności na poziomie systemowym może przynieść ze sobą nowe strategie terapeutyczne ukierunkowane na efektywniejsze przywracanie utraconych funkcji. Może to pomóc ukierunkować badania i praktykę kliniczną na większą efektywność i lepsze wyniki funkcjonalne w rehabilitacji neurologicznej oraz podwyższyć jakość życia pacjentów.

Modele obliczeniowe procesów związanych z neuroplastycznością na poziomie systemowym mogą być pomocne w wyodrębnieniu możliwych jej mechanizmów. Artykuł stanowi próbę oceny, do jakiego stopnia są wykorzystywane obecne możliwości z uwzględnieniem własnych koncepcji, badań i obserwacji.

Introduction

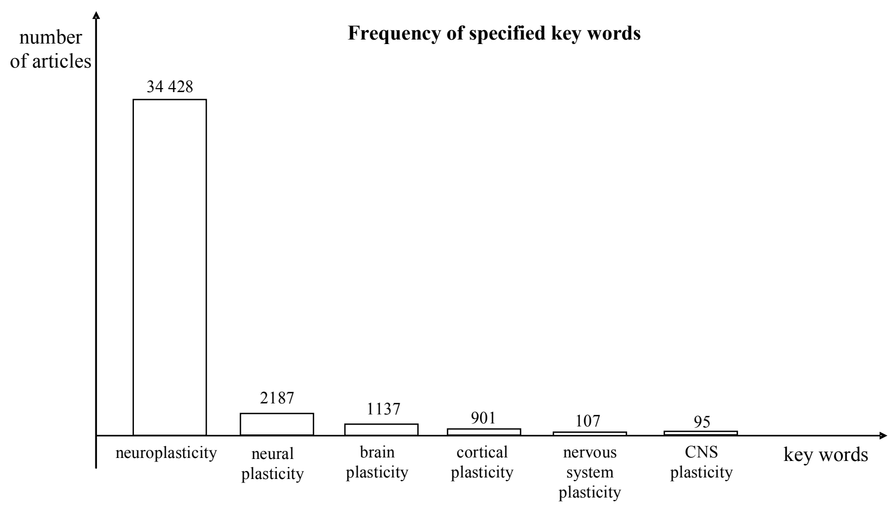
Neuroplasticity (brain plasticity, cortical plasticity) was introduced by Polish scientist Jerzy Konorski [1, 2]. It is perceived flexibility of a nervous system - an ability to be changed (both in functional and structural areas) by processed signals (i. e. through activity, changes in environment, etc.). Neuronal activity associated with particular function (even: whole location of this activity within hemispheres) may change. This is a result of the nervous system reorganization during normal performance (e. g. shaped by environment) or damage. Undelaying mechanisms are complex and widespread anatomical, physiological, and biochemical changes within the (survived) neural circuits. This phenomenon is perceived basis of learning, memory, developmental changes, and compensational changes thanks to neurorehabilitation after nervous system damages, etc. [3, 4, 5, 6, 7]. Developed into effective clinical approaches (neurorehabilitation methods) it allows for partially reinstate cortical representations lost after lesion and provide (at least partial) recovery in persons with a chronic disease or disability due to severe neurological disorders.

Integration of theoretical knowledge and clinical experience concerning neuroplasticity held within neurosciences need for understanding and consolidation of common theories (concerning various levels of processing) and current research [8 , 9]. Computational models of processes associated with neuroplasticity on system level may be useful tool to do it. This article aims at investigating the extent to which the available opportunities in this are being exploited, including own concepts, research and observations.

Current knowledge

Term "neuronal plasticity" was in 1982 introduced to MeSH (Medical Subject Headings) - NLM controlled vocabulary thesaurus. Neuronal plasticity is defined as "the capacity of the nervous system to change its reactivity as the result of successive activations" [10].

PubMed (U.S. National Library of Health) [11] database was searched to identify relevant articles. The research was limited to the English language articles and encompassed the period from 01.01.1991 to 31.12.2011. Figure 1 shows keywords used in the searches and frequency of specified key words combinations.



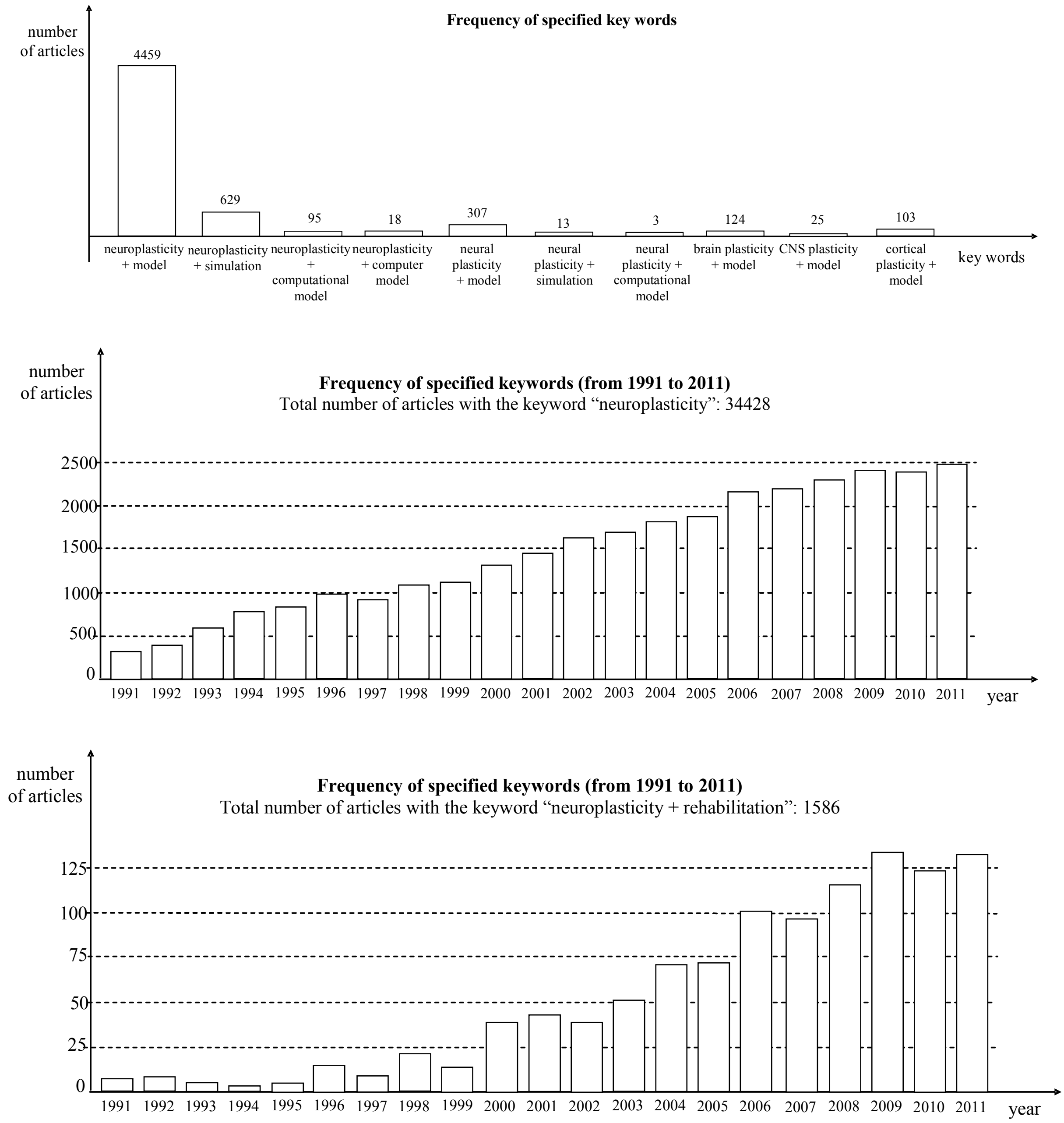


Fig. 1. Results of investigation of the PubMed database (U.S. National Library of Medicine) [11].

Total number of articles with the key word "neuroplasticity" and "rehabilitation" is 1586 constituting only 3,54% of number of articles with key word "neuroplasticity". It makes one of the most important practical application of neuroplasticity – neurorehabilitation - underscored. Rapidly increasing number of articles indicates significant attention paid to this issue by researchers. A distinct feature of NS is its remarkable ability to undergo activity-dependent functional and morphological remodeling via mechanisms of neuroplasticity [12], but abnormal neuroplasticity is perceived involved in such diseases as Alzheimer's disease, epilepsy, dystonia, migraine, schizophrenia, etc. [13]. From the other side neuroplasticity is perceived key element influencing a lot of aspect within health care including:

- influence to memory and other high-level cognitive processes [12],
- therapy of neurodegenerative diseases (e.g. Alzheimer's and Parkinson's diseases),
- neurorehabilitation, especially in stroke survivors, patients after spine cord injuries (SCI), traumatic brain injuries (TBI), etc. [14, 15],

- pharmacology, including non-invasive brain stimulation [13, 16] improving neural functions under pathological states.
- depression, mood disorders therapy [17, 18],
- stress and addiction therapy [19],
- pain therapy [20, 21],
- general anesthesia solutions [22],
- invasive brain stimulation application, etc.

In contemporary neurorehabilitation exercises seems be key issue inducing cascades of processes both on molecular, cellular, system, and behavioural levels supporting brain plasticity [15]. But currently we do not know exactly, how physical exercises (their particular type and intensity) promote e.g. increase peripheral levels of brain-derived neurothropic factor (BDNF) [14]. No doubt motor training (physical therapy interventions) plays key role within this process, supporting spontaneous recovery. But the neural correlates of this activity are not fully explained, despite research both in animals (with cortex lesions) and in humans (using fMRI, TMS, etc.). There is a lot of similar key issues in the area of neuroplasticity which need for further investigation and newer tools. What more some of mechanisms of neuroplasticity may correlate with specific methods used in everyday clinical practice in rehabilitation of patients with CNS deficits: NeuroDevelopmental Treatment-Bobath (NDT-Bobath), Proprioceptive Neuromuscular Facilitation (PNF), Constraint-Induced Movement Therapy (CIMT), Transcranial Magnetic Stimulation (TMS), etc. [8, 9]. Response of the nervous system to inputs, both natural (even altered), and artificial need for another consideration and deeper research. Processing of altered (natural or artificial) signals based on neuroplasticity still seems great challenge to scientists and clinicians. But ultimate goal remains the same: enhancing clinical outcomes thanks to neuroplasticity.

Computational approaches to neural plasticity

Complexity of mechanisms undelying neuroplasticity is remarkable. Synchronization of changes on all levels of processing within NS needs for simulataneous analysis of e.g. structural remodeling of neural networks activated during learning, activity-driven modifications of synaptic strenght, their contribution to neurogenesis (birth and growth of new neurons), neurons death, synaptic elimination or weakening, and synaptogenesis (the growth of new synaptic connections and synapse remodeling). A lot of hypotheses existing in the area of the neuroplasticity make neuronal stimulation-based therapy and functional organization of remaining cortical tissue difficult field for research.

Neural reorganization may be observed on each level of signals processing in the NS, but due to aforementioned complexity computational models of processes associated with neuroplasticity on system level may be especially useful for deriving at least possible mechanisms. Simplified models on system level may enhance our ability to describe them, including contributing factors (biologically plausible). Known this way mechanisms, developed, may further be exploited in more detailed models on other levels.

We should be aware of advantages and disadvantages of computational models. They can provide effective, quick and rather cheap solutions joining theoretical knowledge (even hypostheses) and experimental research. What more models provide occupation for testing and selection of various hypostheses, even not fully possible in the real world (e.g. separate lesions), higlighting the most important mechanisms or simplifying them. This way computational models may reflect mechanisms of neuroplasticity both in the healthy and lesioned brain. But construction of well fitted models is difficult, and needs a lot of experience. What more technical limitations can make models hard to assess, and lack of standarization makes compartment of results difficult [23]. Higher levels of processing require analysis of effective dynamic range, and flexibility of representations. Additionally reorganization of nervous system may be affected by causes (and associated features of the lesion), patients age, type of reorganization (perilesional, remote), and a lot of other factors. Moreover outcomes of clinical assessment (clinimetrics, Functional Magnetic Resonance Imaging - fMRI, Computed Tomography – CT, etc.) may significantly influence effectivity of the therapy.

Basic solutions in computational neuroplasticity modelling on system level are as follows:

- Self-Organizing Maps [24],
- Hebbian networks [25],
- attractor networks [26, 27, 28].

Research in the area of computational neuroplasticity simulation on system level are not so popular as the others: models of synapses, neurons and their properties. Detailed simulations of Pearson et al. [29] are still challenge for a lot of scientists, despite 25 years of use. Further models of Reggia et al. [30] are still used too.

Self-Organized Maps

Self-Organizing Maps (SOMs, also called Kohonen networks) with lateral inhibition may be very useful for modelling pattern recognition processes in the brain. Use of SOMs, trained in an unsupervised mode, may give quick effects because of simplicity. Due to correct output cannot be directly defined, thus computational assessment of the magnitude of the mapping error is not possible.

Müller provided several experiments with modified SOMs (DCNG-SOM) in neurobiological simulations avoiding two main disadvantages: time dependent adaptation procedure and consuming a whole set of disposable neurons [24]. Despite it unsuitable practical application of DCNG-SOM was wide discussed.

Neural Networks with Hebbian Learning

Hebbian networks are classic neural networks with Hebbian learning. They may be useful tools for neuroplasticity simulation [25]. Robertson and Murre proposed three possible post-lesional cases (corresponding with e.g. post-stroke diagnosis based on outcomes of CT or fMRI):

- small loss of connectivity with tendency to autonomous recovery,
- potentially rescuable lesioned circuits, where is possible guided recovery ("neurorehabilitation") using dedicated signals, adequate levels of arousal, and avoiding activation of competitor circuits,
- major loss of connectivity leading to permanent loss of function – there is neef for compensatory approach [31].

This approach proved its efficiency in neural networks models [31].

Attractor networks

Attractors networks are characterized by neurons with excitatory interconnections settling into stable pattern of firing. For this moment attractor networks are used mainly in realistic simulations of memory, especially long-term and working memory [32, 33]. Strenght of synaptic connections may be adjusted using activity-dependent mechanisms (similar to some features of neuroplasticity). Memory dynamics in attractor networks is under research. But attractor networks are still not fully understood and need for large networks of spiking neurons.

Cortical reorganization influences both to only structures and associated functions, but also neural net behaviour. This behaviour may be assessed using computational analysis of attractors baisins and trajectories. Useful solutions are perceived various MultiDimensional

Scalling (MDS) techniques, including Fuzzy Symbolic Dynamics (FSD) - own tool developed in Department of Informatics at NCU [26, 27, 28]. Data similarities and dissimilarities may be derived this way, even through simple three-dimensional (3D) visualization or in a graph. What more, in selected cases, MDS may provide real time neural population monitoring, useful in advanced projects concerning e.g. human cognitive abilities. Depends on directions of further development within neuroscience it may be first step towards next generation of simple diagnostic tool for medicine.

Directions of further research

Current theories (dendritic branching, synaptic plasticity, etc.) are perceived key elements of further computational models of neuroplastical processes. Not fully exploited areas of research seem be:

- mathematical models, still perceived complicated [34],
- models based on liquid state machines (LSMs) reflecting nervous signal processing as distorsions within "liquid" nature of the whole system (e.g. mammalians visual system simulations) – particular attention should be put on possible diversity of the elements and variability of mechanisms and their features [35, 36, 37, 38],
- models of cells death [39],
- models of neurogenesis in adults [40].

No doubt deeper understanding of the relationships between mechanisms of neural plasticity and associated changes in behavior may significantly influence the development of novel, more effective interventions. From the clinical point of view knowledge on neuroplasticity might be applied to therapeutic strategies in neurologically impaired patients. Moreover increased understanding of mechanisms underlying this adaptability can be basement for a new treatments, diagnoses, and prognoses. This may be important due to:

- current biopsychosocial and holistic approach within health care and social care,
- patient-oriented therapy and problem-solving approach,
- common tendency to increase patients quality of life (QoL), especially in disabled, severely ill and elderly patients [41],
- thanks to more effective therapy in basic diseases - possibilities to better help patients with associated diseases, e.g. kidney diseases [42], circulatory system diseases [43], etc.

Conclusions

Better understanding of the mechanisms underlying neuroplasticity on the system level may benefit newest therapy strategies designed to more effectively promote recovery of function. It can help guide and focus research and clinical practice to greater efficacy and better functional outcomes in clinical rehabilitation and increased patients quality of life.

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Received: 24.09. 2012.
Revised: 24.09. 2012.
Accepted: 25.09. 2012.