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Neural Connections and Mental States: The Need for a Neurocognitive Framework

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Abstract

The extensive research into the functional connectivity of the human brain – the human connectome – holds significant promise for the understanding of both the normal brain and a broad range of neurological conditions. There is, however, a growing realization that the human connectome research faces a number of challenges that need to be addressed in order to harvest the full potential of such research. Some of the major issues to be addressed have been emphasized as being: (a) Scales, (b) Individual variability, (c) Structural plasticity, and (d) Structure-function relationship. In the present communication it is argued that an important contribution to the solution of such problems is to conduct human connectome research within the framework of integrative models bridging neural connections and mental states via a computational level. As an example of such an approach the REF (Reorganization of Elementary Functions) framework is presented. The REF framework (the original REF model, the REFCON and REFGEN models) emphasizes dynamic and integrative processes as well as the importance of situationally and experience-dependent strategies. With such an emphasis, this framework appears to be a promising basis for both the design and interpretation of human connectome research.

Keywords: *Human Connectome; Neural Connections; Cognition; Mental States; Neural States; Computational States; Consciousness; Neurology; Brain Injury; Integrative Models; REF Framework; Reorganization of Elementary Functions (REF); REFCON (Reorganization of Elementary Functions and Consciousness); REFGEN (General Reorganization of Elementary Functions)*

Abbreviations

AM: Algorithmic Module; AS: Algorithmic Strategy; EF: Elementary Function; GAS: Goal Algorithmic Strategy; PAM: Perceptual Algorithmic Module; PAS: Perceptual Awareness Scale; REF: Reorganization of Elementary Functions; REFCON: Reorganization of Elementary Functions and Consciousness; REFGEN: General Reorganization of Elementary Functions; SAS: Situational Algorithmic Strategy

The human connectome and the study of neurological disorders

Within the last decade the combined use of neuroimaging techniques and computational methods has caused optimism regarding the possibility of mapping a "functional connectivity" of the human brain – the human connectome [1-12]. Such research has important implications for the understanding of the functional organization of the normal brain – as well as aspects of a range of neurological (as well as psychiatric) diseases. Attempts to use connectome-based research within neurology are for instance found in studies of Alzheimer´s disease [13-17], amyotrophic lateral sclerosis [18] and a spectrum of other neurodegenerative conditions [19].

It is clearly important to integrate the growing understanding of the human connectome into the research regarding the neurological diseases. But in order to be of optimal service to the clinical practice and research, the understanding of the connectome needs to include

an improve possibility to integrate our understanding of on the one hand neural connections and on the other the mental and behavioural states. Such a need has also been stressed by for instance Kelly., *et al* [20].

Presently we argue that the development of truly integrative neurocognitive models is needed in order to solve a number of the problems presently facing connectome research – and not the least being obstacles to utilization of such research within neurology.

The study of the human connectome and its challenges

The gross anatomy of the fiber tracts of the human brain has been known for long [21,22]. The detailed connectivity of our brains has, however, remained rather poorly understood. In animal models, tract tracing techniques have produced an ever-growing body of data regarding the short- and long-range projections of the mammalian brain (including non-human primates) [23-28]. In spite of interspecies similarities much of the connectivity of the human brain does, however, remain obscure. The mentioned research into the human connectome holds promises to remedy at least some of these shortcomings. But in order to make the current connectome research relevant to the understanding of both normal and pathological conditions a significant number of methodological as well as conceptual issues have to be addressed.

Human connectome research has made progress regarding the accumulation of data and identification of patterns of "functional connectivity" – including the development of databases of connectome-relevant data [6,29,30]. It is, however, becoming obvious that the mapping of the human connectome is facing technical as well as conceptual challenges [30,31]. Sporns [31] points to four areas within which human connectome research is confronted by unresolved problems. These are: (a) Scales, (b) Individual variability, (c) Structural plasticity, and (d) Structure-function relationship. Woolrich and Stephan [30] emphasize the importance of addressing structure-function relationships. They point to the need to consider the functional connectivity as a context-sensitive pattern that is modulated by the task faced by an individual. Furthermore, they stress the critical role of biophysical network models when attempting to meet the challenges facing connectome research.

We agree that it is important to address the mentioned areas of challenges. And that it is essential to develop relevant computational – neurocognitive – models in order to conceptualize the human connectome in a meaningful way. We expect that development of relevant neurocognitive models – such as the presently presented framework – will clarify and contribute to the solution of the issue of structure-function relationships. As well as help solve issues regarding scales, individual variability and structural plasticity.

Regarding scales, Sporns [31] primarily focuses on two issues: the anatomical "level" at which the analysis of the connectome should be performed and the issue of "node definition". Since all levels of structural connectivity are likely to matter regarding the functional organization of the brain, it could be argued that ideally a connectome should be described at the level of individual synaptic connections. However, the methods that can presently be applied to human connectome research necessitates that the chosen anatomical level is above those of individual synapses and individual neurons. Within the technologically available anatomical levels, however, it is important to delineate and select functionally relevant anatomical entities as "nodes" for the selection – to perform the network and connectivity analyses based on relevant units/nodes. The importance of adequate delineation and selection is emphasized by Sporns [31] and others [32]. Most connectome research emphasizes a bottom-up dominated approach [33]. The "node definition" in the form of delineation and selection of meaningful nodes is, however, one example of the need for the inclusion of "top-down" elements – in which neurocognitive models may play an important role. Sporns [31] concludes that the parcellation into nodes may be optimal if performed according to multiple structural and functional criteria – pointing to the parcellation of the left lateral parietal cortex performed by Nelson., *et al*. [34] as an example. That parcellation is based on multiple criteria regarding parameters from both resting-state studies and cognitively oriented studies addressing recognition memory. In order to obtain the most functionally relevant node definition and parcellation of the human brain new and comprehensive neurocognitive models may be a necessary tool – and a guideline regarding subsequent interpretation of data.

Variability between individuals may reflect a multitude of courses – including genetic variability. However, it does seem relevant to combine aspects of what Sporns [31] presents under individual variability and structural plasticity, respectively. As stressed by Sporns [31] even brief periods of sensorimotor or cognitive training are associated with structural changes within both the grey and white matter of the brain [35-41]. Additionally, individuals with a specific experience can be shown to have undergone neural reorganizations (even when not exposed to the formalized training used in the mentioned studies). One such example can be seen in orchestral musicians. The Broca area of the frontal neocortex is consistently found to be associated with expressive language and grammar-related processes [42]. In professional musicians, however – contrary to in musically naïve individuals – the Broca area is also involved in mediation of aspects of mental rotation [43]. Apparently, musical training (potentially related to the sight-reading of music) reorganizes the networks – and distributed computations associated with mental rotation – in such a way that the Broca area becomes involved. Such a demonstration of an experience-associated change in the involvement of a cortical area in mediation of a cognitive task does not in itself demonstrate the underlying structural changes. It is, however, reasonable to assume the involvement of modified connectivity at the functional and structural level. Mapping the human connectome without considering the functional and structural individual differences associated with short- and long-term experience would be a highly impoverished project. Sporns [31] seems to be expressing the same sentiments. Studies of experience-associated changes within the neurocognitive organization of the brain may be attempted without the framework of dynamically oriented neurocognitive models. But we believe that both the design and not the least conceptualization of results will gain from the employment of appropriate models.

The area within which the need for neurocognitive and algorithmic models may be most obvious is the last of the areas emphasized by Sporns [31]: the structure-function relationship (also considered in the connectome context by for instance Woolrich and Stephan [30]). As mentioned, it may be important to employ specific cognitive activities during which to measure the patterns of connectivity – and also to address the consequences of cognitive experiences outside of the experimental situation. In both instances a neurocognitive framework may provide important guidelines regarding the specific tasks and circumstances to address. Often the experimental approach has been to measure a "baseline connectivity" defined as the patterns present during a state of rest. In some instances the architecture of connectivity appears rather similar during rest and some types of activation [44,45]. But even if the pattern of connectivity at a given point in time is sufficiently stable to be equally demonstrated under rest and functional activation, it does not eliminate the broader need for considering the cognitive experiences of an individual. It has, for instance, been demonstrated that learning modifies the pattern of spontaneous activity in the resting human brain [46].

In order to make the mapping of the human connectome truly functionally relevant, the patterns of connections need to be related to the level of mental phenomena, behavioural activities and cognitive processes. Maybe it is in this process of relating the obtained pattern of neural/functional connections (the connectome) to mental phenomena that neurocognitive algorithmic models are needed the most. Regarding the process of relating neural circuits and connections to behaviour or mental states, Carandini [47] has argued that the explanatory gap between these two levels is too wide to obtain a reasonable link. He insists on the need for an "intermediate level". And that computations based on neural processing provide a language for theories of behaviour so that computations form such an intermediate level. These arguments resemble the classic levels suggested by Marr [48,49]. Marr proposed three levels of analysis: 1) a computational level, 2) an algorithmic level, and 3) an implementation level. There may be disagreements regarding how to characterize and term the levels, but these and other models converge on the idea that one or another type of algorithmic intermediate level is needed in order to bridge the neural and mental/behavioural levels of analysis. We have previously [50] addressed this issue in detail.

How to approach an intermediate level

The intermediate level cannot be studied without an explicit reference to at least one and most likely both of the neighbouring levels. The overall approaches to the level of computational states differ between the models of Marr [48] and Carandini [47]. The algorithmic level of Marr primarily consisted of computational steps deduced from theories about cognitive operations likely to subserve the processes observed at the level of mental states. In contrast, Carandini primarily assumes the level of computational states to be constructed on the basis of direct neural experimentation (primarily electrophysiological recordings).

When one is to develop an algorithmic model regarding a given neural system, a primary issue is to determine the cognitive domain to focus on. In the close proximity of the input and output pathways of the brain, the connectivity of neurons and substructures may in itself be a proper guideline. The information processing performed by rods, cones, bipolar cells and ganglion cells in the retina, for instance, is relatively well understood [51]. The analysis of such information processing has obviously been eased by the fact that there can be little doubts about the overall functional task of these cells. The luxury of such an understanding quickly disappears as we progress to the vast majority of the circuitry of the brain.

A number of promising approaches to the construction of a computational level on the basis of detailed analysis of the neural circuitry are found within sensory systems – allowing the analysis to be based on that knowledge [52-62]. Another example focuses on the circuitry associated with specific muscular contractions [63]. Such studies with a focus on the relatively early stages of input analysis or the circuitry associated with specific muscular contractions can reveal interesting computational principles. But the methods employed may not be easily applicable to the study of neural systems associated with more advanced cognitive processes/mental states.

There are, however, examples of development of computational models within "purely cognitive" domains. An example is the analysis of spatial orientation-associated systems within the hippocampus and the parahippocampal cortex: the grid cells, border-cells and head-direction cells of the medial entorhinal cortex and the place cells of the hippocampus [64]. The association between on the one hand the hippocampus (and its closely associated parahippocampal regions in the entorhinal cortex) and on the other hand the processing of information relevant to spatial orientation primarily grew out of lesion experiments in which hippocampal injury was associated with impairments of spatial orientation and learning [e.g. 65 – for a review of the early lesion studies: see 66]. Once the consequences of focal lesions had indicated a hippocampal role in the mediation of spatial orientation, a path had been opened to the electrophysiological scrutiny of hippocampal activity in freely moving animals subjected to various types of environments and spatial tasks [67,68]. Mainly on the basis of such electrophysiological studies an extensive mathematical modelling of these systems has been performed. Major efforts have gone into models attempting to analyse how information from grid cells may feed into place cells – providing the latter with their characteristics [69,70]. Additionally, modelling has attempted to construct a computational level which can in broader terms account for the hippocampal and parahippocampal neural processes associated with spatial cognition [71-76]. These are examples of successful development of computational models. But they also illustrate the value of the lesion experiments first demonstrating the association between these neural systems and spatial cognition. In general, we see the study of brain injury and brain injury-associated processes as a crucial tool in the research addressing a computational level. But the study of brain injury is far from a straightforward and simple tool.

Modelling a computational level

The analysis of the consequences of brain injury has for decades been used as a guideline in restructuring many of our cognitive conceptualizations [77,78]. Alongside neuroimaging addressing focal neural activity during task performance, such studies have been and still are the backbone of cognitive neuropsychology. In a critique of cognitive neuropsychology, Patterson and Plaut [79] state that in their opinion the emphasis on single case studies as well as the primary focus on functional dissociation has led to a situation in which cognitive neuropsychology has contributed very little to the understanding of the functional organization of the brain. Coltheart [80] defends cognitive neuropsychology primarily by stressing that the goal of that discipline is not to provide an understanding of the brain – but rather to study the architecture of cognition.

It may, however, be possible to circumvent the problems raised by Patterson and Plaut [79] – and not give up on the idea that cognitive neuropsychology can give rise to important insights about the brain as well as cognition. This requires a modified approach to the study of brain injury [50,81-88]. Some of the major methodological and conceptual differences between this modified approach and the approach described and criticized by Patterson and Plaut [79] can be summarized in the following manner:

- Rather than focusing on functional dissociations seen in single case studies of brain injured patients, the main focus is on experimental studies – in animal models and in humans (intact subjects as well as brain injured individuals).

- Instead of only analysing the primary impairments caused by a particular lesion, the strategy specifically aims to develop models able to explain neural and cognitive mechanisms mediating posttraumatic functional recovery – while they at the same time are able to explain the primary impairments.
- When addressing the cognitive processes associated with initial trauma and not least the recovery process, the focus is as much on "how" as it is on "how well" [82,88]. So rather than establishing the presence or absence of impairments, the analysis scrutinizes the cognitive mechanisms as strategies towards a goal. This holds for patients [89] as well as in animal models [90].
- The conceptual basis for such a research program is neither explicitly nor implicitly the traditional "modular" theories [91-93].
- At the neural level a primary focus is on the rewiring of the brain. This is done regarding reorganizations in the immediate vicinity of the site of injury as well as regarding changes in the long-distance projections [94].

Neuroimaging techniques are employed to reveal changed patterns of regional activation in the recovering patients. Such studies have, for instance, indicated the involvement of right hemisphere mechanisms in the recovery of language in patients suffering aphasia after injury to the left hemisphere [95-98]. It has to be remembered that posttraumatic changes in activity within a given structure may be the consequence of any trauma-related process – e.g. "disinhibition" due to lack of input from the injured brain region. In some instances, however, the patterns of change point more clearly to right hemisphere structures as contributors to mediation of recovery [99].

Extensive animal model based studies have mapped out reorganizational processes after focal brain injury. A few examples illustrate such results. Hippocampal lesions in rats provoke an impairment of both allocentric mapping type spatial orientation [90] and egocentric orientation [100]. In both types of spatial orientation, the posttraumatic impairments are followed by a functional recovery that leads to a full proficiency of task solution. In case of mapping type allocentric orientation, the recovery process can be mediated by mechanisms within either the prefrontal cortex or the parietal association cortex [90]. In case of egocentric orientation, recovery processes can be mediated by the prefrontal cortex [100]. The acquisition and performance of a behavioural task requiring non-mapping type allocentric spatial orientation is apparently left unaffected by both hippocampal lesions [101] and scopolamine-induced inactivation of cholinergic mechanisms (leaving both the hippocampal formation and other acetylcholine-dependent structures inoperable) [102]. In case of both the hippocampal injury and the cholinergic inactivation, the unimpaired task performance does, however, not reflect a lack of normal mediation by the hippocampus and the cholinergic systems of the brain. Instead, the absence of hippocampal/cholinergic contributions to task mediation is immediately "compensated" by dopamine-dependent mechanisms within the prefrontal cortex [101,102]. All of the posttraumatic reorganizations of the neural substrate of task solution are associated with a (more or less) full proficiency of task performance. Scrutiny of the underlying cognitive mechanisms does, however, reveal that within a given task mediation by the various neural substrates are associated with different types of information processing [90,100,103,104].

Such human and animal model based studies point to two important principles. (A) A surface phenomenon such as task performance or conscious representations may before and after injury, respectively, be mediated by dissimilar neural substrates and computational processes – although the surface phenomena superficially viewed are similar (e.g. demonstrating task performance of similar proficiency). Furthermore, (B) contributions to task mediation provided by individual substructures appear to be of a "modular" nature – contributing information processing which is not task-specific – or for that matter specific to any of the cognitive domains – but rather contributes the same type of analysis within a multitude of different contexts/tasks [81,83-88].

On the background sketched above, the mechanisms behind a specific task solution may be seen as a connectionist network combining modular processing units. Thus, it is optimal to operate with not only one computational level, but two such levels: One level at which the computations are those provided by the local networks within substructures of the brain. And a "higher" level at which mental representations are mediated by a connectionist network combining the specific modules of the previous level [105]. We have – in the form of the REF (Reorganization of Elementary Functions) framework developed such a novel approach to the construction of a computational level and an alternative understanding of modularity [81,83-88,105-107].

A framework bridging neural connections and mental states

The original version of the REF model [81,83-88] primarily focuses on the mechanisms of problem solving as well as the neural and cognitive processes mediating posttraumatic functional recovery after focal brain injury. But as importantly: the original REF model provides the basic reconceptualization of neurocognitive organization which forms the basis for the entire REF framework.

The "modular" element within the REF model is the Elementary Function (EF). EFs are strictly localized in the sense that each EF is mediated by a local (and relatively small) neural substrate within a substructure of the brain. Typically, every structure or substructure of the brain (e.g. the hippocampus) constitutes the neural substrate of hundreds or thousands of EFs. An EF provides a fixed information processing in the sense that it receives an input, performs the given informational transformations and provides an output. EFs are not specifically associated with any of the traditional cognitive "functions" (such as attention, allocentric spatial orientation or language production). Rather, practically every EF participates in distributed networks mediating a multitude of surface phenomena and thereby typically contributes to what is traditionally seen as several if not many "cognitive functions". The information processing of an EF is best expressed in mathematical rather than cognitive terms.

The bridge between the basic information processing of EFs and the surface phenomena in the form of behavioural manifestations, mental representations, etc. are the Algorithmic Strategies (ASs). ASs are connectionist networks combining EFs into the "programs" mediating surface phenomena. An important difference between ASs and most of the more traditional connectionist networks [108-111] is that while traditional connectionist networks operate with a "unit" representing a functionally neutral "neuron", the ASs of the REF model are connectionist networks combining advanced processing units in the form of EFs. Most, if not all, ASs are established on the basis of experience and the feedback obtained when attempting problem solving. The result of a given attempted task solution leads to a backpropagation mechanism [112-114]. These backpropagation mechanisms modify the connectivity within ASs and via such experience-driven processes, ASs are optimized according to the experience of the individual and the current situational demands. That is: In any given situation, a "best guess" AS is activated and becomes the mechanism of task solution. The outcome of the attempted task solution is then compared to the current goal. The outcome of this comparison leads to two further processes: (1) In case of success, the applied AS will in the future be re-applied in similar situations – in case of failure an alternative AS will be engaged. (2) A backpropagation process modifies the connectivity between EFs according to the relationship between the goal and outcome – a process potentially creating novel ASs.

An additional "level" is included in the original REF model in the form of Algorithmic Modules (AMs). AMs are – like ASs – connectionist networks combining EFs. They do, however, differ from ASs by not in themselves being able to mediate surface phenomena. An AM is rather to be seen as an advanced "building block" for ASs. Typically, an AM will emerge as a "common area" of several ASs. As an example, processes such as language production or language interpretation are mediated by ASs – strategies allowing the surface phenomenon of production or interpretation of language, respectively. In contrast, an element such as grammar may be mediated by an AM [115]. Grammar is of course an important element within language – but grammar cannot in itself constitute a surface phenomenon. The original REF model has recently been reviewed in Mogensen and Overgaard [105].

In order to expand the REF framework into the areas of perception and conscious awareness we developed the REFCON (Reorganization of Elementary Functions and Consciousness) model [106,107]. The REFCON model is based on the same basic units and principles as the original REF model – but contains a number of important expansions. Two of these are the Perceptual Algorithmic Modules (PAMs) and a specialized AS named the Situational Algorithmic Strategy (SAS). The REFCON model have recently been summarized in Mogensen and Overgaard [105].

PAMs are hierarchically ordered AMs representing the external objects to be perceived. PAMs at the lower levels will mainly represent "features" of such objects while PAMs at the higher levels are progressively more specific regarding representation of what is being perceived. Selection of PAMs in a given perceptual process takes place in a "mutual competition" that eventually will result in selection of a PAM of the highest level. Being AMs, however, PAMs cannot in themselves be the mechanism of the mental representation of what is being

perceived (including the conscious awareness of such a percept). It is only by becoming integrated into SAS that PAMs of the highest level become available to conscious awareness and as the basis of action.

SAS is a specialized and highly dynamic distributed network reflecting the current status of the individual. SAS is represented within practically all (if not all) regions of the brain – and represents both the current stimulus situation (external world) and the current "internal" status of the individual in the form of for instance thoughts and other mental representations.

It is the degree of integration into SAS of a given PAM (or for that matter other AM) that determines the level of conscious awareness of what is represented. Traditionally, perceptual awareness has been considered in a dichotomous way. Consciousness has been considered to be either present or absent. The use of more refined methods – e.g. the Perceptual Awareness Scale (PAS) [116] – has documented that consciousness is better understood as being present in degrees [117-120]. And it is the degree of integration into SAS that is the mechanism of such "levels" of conscious awareness.

The most recent development within the REF framework is the REFGEN (General Reorganization of Elementary Functions) model [105]. The REFGEN model expands both the original REF model and the REFCON model into an overall modelling of neurocognitive organization and functioning. The REFGEN model thus avoids some of the shortcomings and under-defined entities typically being included in more domain-specific and restricted models (such as the original REF model and the REFCON model). The REFGEN model includes all the elements mentioned under the two previous models but adds two additional, specialized ASs: GAS (Goal Algorithmic Strategy) and Comparator.

In parallel to SAS, GAS is a highly distributed and extremely dynamic AS. But while SAS represents the current status of the individual, GAS represents the current "goal configuration". "Goals" include both very specific and limited short-term goals and more overall and long-term goals. Short-term goals may be the need to manipulate the environment in a particular way or to specifically gather information within a limited part of the visual field. While more general and long-term goals represented within GAS may take many forms.

Comparator is a specialized AS that constantly compares SAS and GAS. On the basis of such comparisons, Comparator may initiate a broad range of processes. Some such processes are externally oriented behaviour mediated by activation of "ordinary" ASs. But Comparator also initiates backpropagation-mediated restructuring of both SAS, GAS and Comparator itself.

The restructuring of ASs – including SAS, GAS and Comparator – demands both short-term and more "permanent" synaptic modifications. While some ASs may be structured on a semipermanent basis, dynamic changes within SAS, GAS and Comparator will often require a rapid and short-term "attachment" and "de-attachment" of individual EFs into one of these ASs. As discussed in detail by for instance Mogensen and Overgaard [105] some of the potential mechanisms for such rapid reorganizations may be prewired "latent" synapses [121-124] as well as modifications of dendritic spines [125-132].

A common feature of all models within the REF framework is that experience-dependent reorganizations of the connectivity between EFs constantly modify both the strategies of task solution and the ways information is represented. Thus, this framework emphasizes dynamic processes adapting the neurocognitive connectivity according to environmental circumstances and the experience of the individual.

Addressing the human connectome in the context of the REF framework

We believe that the REF framework is well-suited as a frame of reference regarding both the design of human connectome experiments and the interpretation of results from such studies.

Within the REF framework important information may be gained by addressing both intact individuals and neurological patients. In the context of the REF model the neurological conditions most frequently addressed is focal acquired brain injury. One of the motivations

for the development of the original REF model was to obtain a neurocognitive model that can simultaneously account for both functional localization and posttraumatic functional recovery. According to the REF model, functional recovery is mediated by the backpropagation-driven reorganization of ASs. When a patient is affected by acquired brain injury, the tissue lost to brain injury is lost forever. Consequently, the EFs mediated by the affected brain tissue are also chronically lost. Thus, all ASs including those EFs are lost. And, consequently, the surface phenomena mediated by those ASs will be either lost or impaired. The subsequent recovery process, however, will include attempted task solution by application of whatever (more or less relevant) ASs are available. Associated with such attempted task solution backpropagation mechanisms will modify ASs. Such modifications will in most instances eventually shape ASs that can mediate surface phenomena that appear closer to if not identical to the pretraumatic situation. If the recovery process leads to a surface phenomenon of equal proficiency to what was seen pretraumatically, the situation will typically be characterized as a "full recovery". It is, however – as for instance stressed by Mogensen [87] – important to notice that although the patient may be clinically characterized as "fully recovered", neither the neural nor computational mechanisms are identical to the pretraumatic situation.

One highly relevant and promising line of research within the human connectome research will be to address similarities and differences between normal and more or less recovered brain injured individuals. And highly important information may be gained by studies that follow longitudinally the reorganizations associated with recovery processes in patients suffering acquired brain injury.

The REF framework differs from most – if not all – other neurocognitive models by a primary focus on "strategies" rather than more traditional cognitive "functions". The traditional focus on cognitive functions (e.g. selective attention, allocentric spatial orientation and expressive language) has in the REF framework been replaced by a focus on the analysis based on ASs – not the least SAS, GAS and/or Comparator. In the context of human connectome research, the REF framework will, thus, call for a focus on the ways in which both experience (the availability of specific strategies) and the acute situational demands (the ways in which specific strategies are recruited in a given situation) influence the patterns of the connectome.

Regarding the issues raised by Sporns [31] (see above) the REF framework, thus, primarily points to studies addressing Individual variability, Structural plasticity and Structure-function relationships. But even regarding Scales, the REF framework may provide a novel approach since the neural substrate of individual EFs may emerge as a relevant scale for the analysis of dynamically changing connectivity patterns.

Perspectives and Conclusion

The REF framework is currently being further developed in a number of ways according to both theoretical considerations and available data. But a closer integration between studies of the human connectome and neurocognitive models such as the REF framework will no doubt be mutually beneficial. It will contribute to both the attempts to create more adequate neurocognitive models and to map and comprehend the human connectome. Only in such an interaction will it be possible to better conceptualize the constantly changing dynamic relationships within the human brain.

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