



## Review

# The specific contribution of neuroimaging versus neurophysiological data to understanding cognition

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## ABSTRACT

The role of neuroscience for the understanding of cognitive processes is a matter of controversial discussions. While it is widely accepted that neuroscientific data do contribute to theories on cognition in some way, their specific value is most often not explicitly described. One central issue is the validity of the inference from neuroscientific data to underlying cognitive processes, which depends on the characteristic properties of the respective neuroscientific method. In the first part of this review, we discuss the conditions under which data from functional MRI (fMRI), surface EEG, and intracranial EEG recordings may be interpreted with respect to associated cognitive processes. We will show that due to the different signal characteristics in each domain, cognitive processes at different levels can be captured. In the second part, we address the *specific* contribution made by neuroscientific data to the understanding of cognition. We show that neuroscientific findings may move beyond psychological theories based on purely behavioral data in several respects, which again depend on the imaging modality. Taken together, we suggest that neuroscientific data contribute to the understanding of cognition by adding specific biological constraints and by extending the explanatory potential of psychological theories.

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## 1. Do we need neural data?

Studies in cognitive neuroscience, like in all branches of neuroscientific research, may tell us a lot about how the brain works. For example, the activation of the hippocampus during long-term memory (LTM) encoding provides information about the function of this brain region (e.g., [71,32,26]), and electrophysiological findings may be related to the rapid synaptic plasticity in this region [22,3]; activation of the prefrontal cortex during maintenance of items in working memory (WM) reveals the functional relevance

of reverberatory activity within dopaminergic prefrontal networks (e.g., [51,75]); and so on. From this perspective, the brain is just one – though particularly complex – organ of the human body whose physiology can be investigated similar to that of, e.g., the liver. Therefore, cognitive neuroscience may be understood as one exciting sub-discipline within the larger field of physiology. Importantly, the main question of this scientific branch is to understand the functional organization of the brain at its various levels, from molecular biology to cells and neural assemblies and finally to the entire brain – the focus is thus not on understanding cognitive processes per se. In addition to this physiological point of view, knowledge about the functional role of a brain region may be extremely important for clinical purposes, e.g., for the interpretation of neuropsychological symptoms in a patient with brain lesions or for the prediction

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of the neuropsychological outcome of neurosurgical interventions. From this clinical perspective, cognitive neuroscience can be seen as an important tool among a wide range of other clinical methods. Results from cognitive neuroscience are complementary to neuropsychological studies in patients with brain lesions, because they reveal brain regions which participate in a task during physiological functioning. Neuropsychological results, in contrast, indicate whether a certain brain region is *necessary* for a task, which may differ from the brain regions contributing to this task under normal conditions. For example, a large network of brain regions shows an enhanced BOLD response during verbal memory tasks, although not all of these regions are crucial for task performance – lesions in at least some of them do not deteriorate task performance, for example due to reorganization of cognitive functions. However, apart from these physiological and clinical viewpoints, it is still a debated question whether neuroscience can also teach us something about the cognitive processes themselves (e.g., [34,17]) and, in case a general relevance of neuroscience is admitted, how the contribution of neuroscientific results to cognitive science can be specified.

In this review, we will first consider a functionalist perspective on cognition, namely that cognitive processes may in principle be studied independently from their specific implementation (in the brain, in computers, robots etc.). From this view, the criterion for the question whether neuroscientific results are informative for cognition is whether these results allow to infer specific cognitive processes. We will discuss the specific problems of this inference for two important techniques in cognitive neuroscience, functional MRI (fMRI) and EEG (including scalp and invasive electrophysiological recordings). Our arguments will be mainly based on results from memory research, because this is the authors' main field of research; in principle, however, the arguments in this section also apply to other domains of cognitive neuroscience. The empirical studies cited are just examples and by no means represent a complete overview of the respective fields of research. Next, we will consider the *specific* contribution of neuroscientific results to the understanding of cognition and show that these contributions are substantially different (complementary) as compared to the contribution of data from behavioral research. These arguments principally question a purely functionalist perspective, because they suggest that a full understanding of cognitive processes in humans requires to take the biological foundations of human behavior into account.

The relevance of neuroscientific data for the understanding of cognitive processes has been already discussed in a number of previous articles; in 2006, the entire issue 3 of the journal "Cortex" was devoted to this question. Here, we move beyond this more general discussion by focusing on two particular questions: First, under which conditions is the inference from neuroscientific data to cognitive functions valid in two important domains of cognitive neuroscience; second, what specific contribution do neural data from these domains make to the understanding of cognitive theories (that cannot come from behavioral data alone).

## 2. The functionalist point of view

Functionalism can be defined as the view "[...] that what makes a mental state the type of state it is – a pain, a smell of violets, a belief that koalas are dangerous – is the functional relations it bears to the subject's perceptual stimuli, behavioral responses, and other mental states." [47]. The lack of reference to brain processes in this predominant perspective in cognitive science thus implies that a given cognitive process may be "implemented" in various different ways, not only in the brain but also in computer simulations, robots etc. Historically, among the first proponents of this idea were Hilary Putnam [56] and Jerry Fodor [27]. Based on a parallelization of cognitive processes and computer simulations, they suggested

that both could be understood without reference to their particular physical realization. The motivation for this theory came from a critique of the "identity theory" (e.g., [69]), stating that mental states are identical with their specific neurophysiological realization; Putnam and Fodor argued that the same mental states may also occur in other organisms with complete different biological properties, or even in artificial systems. Coming from a computer science background, David Marr [49] argued in a similar vein that the algorithms computed by the brain should be analyzed prior to an investigation of their implementation. In a strong version of this perspective, knowledge about brain processes is entirely irrelevant for the understanding of cognitive processes, because these cognitive processes can similarly occur in brains, computers, robots etc. Therefore, the biological details of the brain's architecture and physiology do not play a role in the explanation of cognition – they are just one among many other ways how cognitive processes can be realized. As a result, psychological theories (e.g., on the limited capacity of the WM store) can be established without any reference to the brain.

## 3. The neuroscientific point of view

Proponents of the relevance of neuroscientific data for the understanding of cognitive processes argue that information about the neural basis of a specific task provides additional information about the cognitive processes during this task. Such a neural basis is typically defined either in terms of an increased recruitment of a certain brain region during a task (in the case of techniques with a high spatial but relatively low temporal resolution such as fMRI and PET), or in terms of electrophysiological markers of neural activity (in the case of scalp EEG or MEG recordings, which can be generally conducted in human subjects, and in the case of invasive electrophysiological recordings, which are restricted to specific patient populations). For example, if during an fMRI experiment the blood oxygen level dependent (BOLD) response in the occipital cortex is more pronounced during one condition of a task as compared to another, this is taken as evidence for a more intense visual processing in this condition; activation of the hippocampus is interpreted as showing encoding into or retrieval from declarative LTM; and so on. Furthermore, the time course of neural processing during a task can be investigated with high temporal, but relatively low spatial resolution by scalp and intracranial EEG recordings. In contrast to fMRI, scalp EEG recordings are only suited for the investigation of neocortical activity and do not allow to explore deep brain structures such as the hippocampus. Intracranial EEG recordings in specific patients populations can be used to study the activity of local networks of neurons and even of single cells, allowing for an even closer linkage from cognition to more mechanistic approaches to brain function such as the investigation of synaptic plasticity during learning in animals. In the following, we will focus on fMRI and EEG and discuss their contribution to an understanding of cognitive functions; the same arguments apply also for related methodologies (e.g., PET instead of fMRI; MEG instead of EEG). The validity of the inference from neuroscientific activation patterns to cognitive processes – what has been called "structure-to-function induction" [34] – depends on the specificity of these activation patterns with regard to the investigated cognitive processes. We will thus discuss to what extent results from fMRI, scalp EEG and intracranial electrophysiology can be considered specific with respect to cognitive processes.

## 4. General problems of neuroimaging and neurophysiological studies

Both in functional MRI and in EEG studies, the interpretation of the results with regard to the involvement of a specific cogni-

tive process is hampered by the fact that these results may occur in a large number of tasks, so that they are in no way specific for only one cognitive process (this point has already been highlighted in previous reviews, e.g., [12,2]). It is even possible that activity within a certain brain region supports completely opposing functions depending on the specific context of a task. For example, while activation of the dorsolateral prefrontal cortex is associated with impaired LTM encoding of individual items [55,14], it predicts successful memory formation during relational manipulations of multiple items [6]. Similarly, activation of the parahippocampal cortex during WM maintenance is predictive for subsequent memory if the WM task is executed successfully [64,4], but is associated with subsequent forgetting during unsuccessful attempts to complete the WM task [4]. In other words, the relationship between a BOLD response in a particular region and cognitive processes varies and can even reverse depending on the specific context. Therefore, in many cases the interpretation of activity in a certain brain region requires to take the context into account, which is primarily defined by specific task demands or behavioral outcome (i.e. by associated independent or dependent variables).

It can be argued that this “context” is also reflected in the entirety of neural activity, and possibly also in the pattern of BOLD activations in the brain. This context pattern of activity may, for instance, be investigated using bivariate (e.g., [31,59]) or multivariate (e.g., [33,53]) measures of BOLD activity. In the above example of the equivocal link between BOLD activity in the parahippocampal cortex and LTM formation, we used the single-beta series correlation method of Rissman et al. [59], which revealed that the relevant behavioral context (successful or unsuccessful conduction of the WM task) was related to the correlation of parahippocampal activity with activity in adjacent brain regions: while this correlation was high during successful conduction of the WM task, suggesting integrated and well-controlled neural processing, it was significantly reduced during unsuccessful attempts to complete this task [4]. The ambiguous relationship between parahippocampal BOLD activity and memory formation could thus be resolved by taking the correlation of this activity with adjacent BOLD responses into account.

## 5. Specific contribution and problems of fMRI

Functional MRI is currently the most widely used technique in cognitive neuroscience and has been applied to studying virtually all types of cognitive functions. Its major advantages are that it can be readily applied to healthy human subjects due to its non-invasiveness, that it has a relatively high spatial resolution in the order of several millimeters, and that it allows for the simultaneous investigation of the entire brain, including deep subcortical structures such as the hippocampus or the basal ganglia. Data from fMRI studies rely on the BOLD signal, which depends on blood oxygenation and perfusion and thus on regionally specific modifications of brain metabolism and energy supply. While this relatively direct connection to energy consumption makes fMRI results interesting from a larger perspective (see below, Section 7), it also imposes specific problems for an interpretation of these results in cognitive terms. Several factors complicate a straightforward interpretation of fMRI data. First, a BOLD response may either be due to inhibitory or excitatory synaptic inputs. This issue has been described in a recent review by Logothetis [46]: while an increased excitation results in an enhanced BOLD response if a certain threshold is crossed, an increased inhibition may either also enhance metabolic activity, as found, for instance, in the rat hippocampus [1], or attenuate the BOLD response due to an overall reduction of network activity. As described by Buzsaki et al. [11], this issue is particularly relevant for structures which are tonically active and modulated by inhibitory inputs. One example is

the thalamus, which receives GABAergic inputs from the basal ganglia: because energy consumption and BOLD response are most closely coupled to synaptic activity rather than spikes [45], an increased firing rate in the basal ganglia does not directly affect metabolism in the same region, but enhances energy consumption in the thalamus, although these inhibitory inputs lead to a reduction of thalamic firing rates [19]. Thus, BOLD responses and firing rates are negatively correlated in this case. An even more complex relationship applies in the case of dopaminergic inputs, which may be either excitatory or inhibitory depending on the subtypes of postsynaptic receptors and the level of presynaptic activity [42]. Recently, Schott et al. [65] directly showed that dopamine release in the nucleus accumbens is accompanied by an enhanced nucleus accumbens BOLD response. Reward consumption and expectation increase the firing rate of both dopaminergic midbrain neurons [66] and GABAergic nucleus accumbens cells [67]. Nucleus accumbens neurons project back to the ventral tegmentum, where they inhibit the tonically active dopaminergic neurons and thus establish a negative feedback loop. Interestingly, increased dopamine release in the nucleus accumbens was also associated with an enhanced BOLD response in the ventral tegmentum [65]. Taken together, these studies indicate that an increased BOLD activity in a particular region only indicates enhanced inputs into this region, but cannot be taken as evidence for the direction of this input (excitatory or inhibitory).

Second, the BOLD signal depends on integrated synaptic activity across at least hundreds of milliseconds and thus does not provide information at finer time scales. Thus, the same BOLD response may arise from various different patterns of neural activity. This specific complication is described further below. Third, BOLD responses do not allow to distinguish whether neural activity is correlated, i.e. they are independent of the degree of synchronization of activity within a given region. Only the effects of synchronization – more reliable transmission of information to a downstream region [63] and more efficient communication within neural networks [30] – may be measured indirectly via an increased BOLD response in that downstream region. Fourth, the phase of ongoing oscillatory activity is not reflected in the BOLD signal [24]. It has been shown in several studies that cognitive processes specifically affect (or are affected by) the phase of oscillatory activity. For example, an increased stimulus-related phase locking across trials of oscillatory alpha/beta activity is an important mechanism supporting WM maintenance [60] and LTM encoding [61,25]. In addition to this stimulus-related concentration of phases, several studies reported cross-frequency coupling of the phase of oscillations in a lower frequency range to the amplitude of activity in a higher frequency band (e.g., [52,13,18,15,16]; this mechanism was suggested to be functionally relevant for multi-item memory processes [44,36]; see also last chapter).

To summarize, the interpretation of BOLD activity in a certain region is problematic if cognitive differences are not reflected in the amount of total synaptic input to a particular region (which appears to be the closest neural correlate of the BOLD response), but only by differences in the ratio of excitation and inhibition, in the peculiarity of neural activity on a fast time scale, or in the phase of oscillatory activity. In the second part of this article, we will describe why there are indeed good reasons to assume that this level of detail is relevant for cognition. Based on a similar line of reasoning, it has been argued that only electrophysiological methods which provide information about neural activity with a high temporal resolution index functionally relevant processes [8].

However, an inference from fMRI data to cognitive processes is most likely valid in at least some conditions. Most fMRI experiments only investigate relatively broad cognitive processes – e.g., declarative versus procedural memory formation – and do not distinguish between fine-grained processes such as the specific mental content being memorized (exceptions are recent studies using multivariate

decoding techniques, e.g., [38,33,53,73,40]). It is likely that neural activity supporting these broad processes can be found in wide regions of the brain and not only in a highly localized region or in transient networks defined by very specific temporal activity patterns: The success of neuropsychological investigations of patients with brain lesions shows that the brain is to some extent organized in large modules, e.g., the Brodmann areas. At least in some of these regions such as the primary visual cortex or the Broca area, lesions lead to specific and circumscribed neuropsychological deficits, indicating that they are specifically related to one particular function (no other region may take over this function, and no other function is impaired). This suggests that at this level, brain organization and cognitive processes can be considered modular [28] and may be directly related. Similarly, category-specific regions have been found in the inferior temporal cortex of the ventral visual processing stream (e.g., [39,21]). On the other hand, there are also examples where no modular organization can be found in the brain. For example, while it has been estimated that a large number of around one million neurons in the hippocampus respond to each individual stimulus [76], these neurons are not spatially clustered [58,57]. Due to this distributed stimulus representation scheme and the lack of a topographical organization in the hippocampus, signals originating from the averaged responses of a large number of adjacent cells cannot be expected to reflect processing of specific stimuli or stimulus categories.

## 6. Specific contribution and problems of scalp and intracranial EEG

As compared to fMRI results, data from surface EEG recordings have a high temporal resolution and thus allow to distinguish different neural processes within the same region – although the separation of “regions” is difficult due to the low spatial resolution of this method. Therefore, these data allow to draw inferences on cognitive processes whose neural correlates are specified by their level of excitation or inhibition, by their neural signature (for instance, time-dependent alterations of activity in different frequency bands) on a fast time scale, or by the underlying phase dynamics. However, even though EEG allows to differentiate various activity patterns within a given brain region, the inference from activation patterns in EEG to specific cognitive processes may be equivocal as well. Several cases may be discussed here. First, event-related potentials (ERPs) provide direct evidence about the timing of cognitive processing. For example, during an oddball paradigm, target versus standard stimuli produce an enhanced P300 component [72], but no difference in earlier visual ERPs. This indeed provides some information about the cognitive processes during this task, because it shows that target processing occurs only after early visual processing has been finished. Furthermore, the P3 component could be further distinguished into the P3b component related to the behavioral relevance of this stimulus and the novelty-related P3a component, which is also enhanced by unexpected but behaviorally irrelevant stimuli. In contrast to the P3b component, the P3a depends on the integrity of the hippocampus, which has been clearly demonstrated by a study on patients with hippocampal lesions [41]. Contrary to the case of fMRI, where a BOLD response in a given brain region does not allow to infer whether this response is due to an increased excitation or inhibition, slow neocortical ERPs with negative polarities are indicators of an increased excitation, and ERPs with positive polarity are associated with inhibition (e.g., [70]). This relationship is reflected by behavioral measures: during a Go/No-Go paradigm, slow positive EEG potentials in the NoGo-condition, which required inhibition of a prepared motor response, were associated with a reduced startle reflex [68]. Recently, we summarized findings suggesting that during memory formation, the hippocampus delivers an inhibitory signal to the neocortex and

renders stimulus representations sparser, which is accompanied by positive hippocampal and neocortical ERPs [5].

Second, apart from ERPs, EEG recordings allow to distinguish specific spectral patterns of neural responses. In general, field potentials reflect synchronized synaptic inputs and may occur in different frequency ranges, depending on the precision of neural synchronization. Moreover, in general the size of a synchronized neural assembly is inversely correlated with its synchronization frequency, i.e. larger networks are synchronized at lower frequencies [9]. Methods of time-frequency decomposition (e.g., using wavelets) allow to study the time-varying frequency components of a neural signal. These results are particularly interesting, because oscillatory activity can also be investigated in electrophysiological recordings in animals (and even in vitro). Therefore, inferences from these data on cognitive processes may be inspired by cognitive functions observed in animal research. For example, synchronization of neural activity in the gamma frequency band (>30 Hz) seems to be closely related to attentional and memory functions not only in humans (e.g., [23,35]), but also in animals (e.g., [29]).

However, it should be noted that the inference from activity in a specific frequency band to a cognitive process is not straightforward either. First, oscillations in a certain frequency range may be caused by very different mechanisms depending on brain region, which have fundamentally different relations to behavior; for example, while pronounced neocortical theta oscillations (between ~3–8 Hz) physiologically occur during drowsiness and sleep, hippocampal theta oscillations in a similar range are, for example, associated with environmental exploration. The mechanisms underlying gamma oscillations in the neocortex and hippocampus differ as well [74]. Second, even in individual brain regions oscillatory activity may be related to very different cognitive processes; for example, hippocampal theta oscillations have been related to processes as diverse as arousal, decision making, memory, orienting, anxiety, navigation, and so on [10]. Finally, there is reason to assume that cognitive processes are constrained by the energetic costs of the underlying brain processes (see below), such that energetically sparse processes are privileged. Due to the nonlinear relationship between neural activity and energy consumption, an energetic level cannot be directly inferred from neural activity, however [11]. In this respect, measures of hemodynamic supply such as fMRI or metabolism such as PET may be more directly related to the specific constraints cognitive processes embodied in the brain.

Intracranial EEG recordings allow to bridge the gap between cognitive neuroscience studies in human subjects and more mechanistic approaches to brain function in animal experiments. Due to the invasiveness of this technique, it can only be conducted in specific patient populations, most importantly patients with epilepsy during presurgical investigations and patients undergoing deep brain stimulation. In some cases, not only macroelectrodes are implanted, which average across the activity of large groups of neurons in a certain brain region, but also microelectrodes which are suited for the investigation of action potentials of single neurons. Recording activity from single neurons allows to distinguish neural activity at an extremely fine temporal and spatial scale. However, besides the poor availability of this technique in humans (single-unit recordings are only performed in neurological patients in a few large centers), even here a direct inference from neural activity to cognitive function is questionable, at least as long as only the frequency of action potentials is investigated: It is still a matter of intense debate whether the firing rate of individual neurons is their only property which is required for information processing. Any measure of firing rate integrates over some interval which should be larger than the typical inter-spike interval; therefore, information about the exact time of occurrence of individual spikes is lost. At least in rats, however, it has been shown that the exact timing of individual spikes (with respect to theta phase) may provide infor-

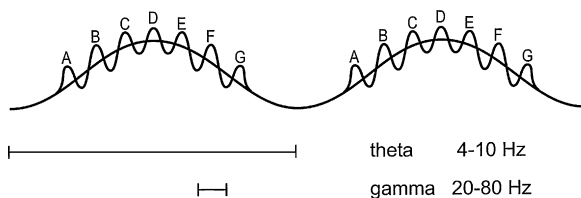


mation on spatial locations [54] and is relevant for putative cellular mechanisms of memory formation like spike-timing dependent plasticity [48].

## 7. The specific relevance of neural data

In the previous section, we have discussed the validity of an inference from cognitive neuroscience results in different domains (fMRI, surface EEG and intracranial EEG) to cognitive processes. We have argued that this inference is actually valid for both kinds of data, but only if suitable cognitive processes are being investigated and if the respective ambiguities are taken into account. In a next step, we will discuss whether these neuroscientific data inform cognitive theories similar to behavioral data, or whether they provide qualitatively different information. Several reasons suggest that neuroscientific results add qualitatively different constraints, which are due to the fact that cognitive processes are actually implemented in the brain instead of in a computer. For example, the brain requires a vast amount of energy (around 20% of the body's energy for only 2% of its mass). Therefore, algorithms that reduce energetic costs are preferable, which restricts information processing in the brain [43]. As described above, while fMRI and PET data are closely related to energy consumption, electrophysiological recordings are not. Several studies actually suggest that cognition is indeed constrained by the demand to be energetically advantageous. For example, BOLD responses in the prefrontal cortex are negatively correlated with individual performance in simple sensory-motor tasks, indicating that high-performing individuals recruit prefrontal resources more efficiently than low-performing subjects [62]. These data suggest that energetically more efficient processes are also advantageous on a cognitive level.

Second, relating cognition with brain processes may help to further explain quantitative psychological findings. For example, the WM store has a restricted capacity of only a few items. While it is still a debated question whether this capacity depends on the material being maintained, it can be measured behaviorally and has been estimated between about two items [20] and seven items [7,50], depending on the exact criterion. However, even if the WM capacity was measured with infinite precision, it would still remain an open question *why* exactly this number of items can be maintained. In other words, the empirical finding of the numerical value of a psychological variable has only a rather limited explanatory power. Neuroscientific data can provide a more fundamental explanation of these empirical findings. In the case of WM, a detailed biological theory has been proposed by Lisman and co-workers [44,37] which has currently still not been demonstrated experimentally, but which makes testable experimental predictions and would, if confirmed, further explain the capacity of WM. According to this theory, each individual item in WM is represented by neural assemblies defined by synchronized gamma band activity. Multiple items are distinguished by the phase of simultaneous oscillations in the theta frequency range (see Fig. 1). For example, if the first item is represented by a gamma cycle at a certain



**Fig. 1.** Maintenance of multiple items in working memory by cross-frequency coupling. According to this model, individual items are represented by neural assemblies synchronized in the gamma frequency range, which occur at a specific phase of theta band activity (figure modified from [36]).

phase of theta band activity, the second item is represented by a gamma cycle at a subsequent phase, and so on (this mechanism would parallel the mechanism of “phase coding” in the hippocampus of rodents during spatial navigation, [54]). As a consequence, only a limited number of gamma cycles fit on one theta oscillation, and this number determines the WM capacity. If this model will be confirmed by experimental evidence, it allows to explain a quantitative psychological finding – the capacity of the WM store – by relating it to underlying neural processes. It further allows for several experimentally testable predictions: for instance, in case of an altered dominant gamma or theta frequency, WM capacity should be modified as well. At least within the hippocampus, the frequency of gamma oscillations depends on the decay time constant of inhibitory postsynaptic potentials [77]; drugs such as benzodiazepines which increase the affinity of GABA to the respective receptor and thus prolong this time constant should decrease WM capacity. Moreover, even if gamma and theta frequency remain constant, WM should deteriorate if the coupling of gamma power to theta cycles is impaired.

Finally, a (principally different) argument for the relevance of neuroscientific data for cognitive theories states that a full understanding of functional processes requires that a connection to the biological mechanisms underlying these functions may be provided. An analogy to other body systems makes this point understandable: even if a complete functional characterization of processes within the liver is given (i.e. a complete description of its relevance for various metabolic processes), one may still demand that the cellular and molecular mechanisms underlying these processes should be given. From this perspective, a complete understanding of cognitive functions requires that also the embodiment of these functions in the brain can be explained. Even if neuroimaging results cannot unequivocally distinguish between two psychological theories, they add relevant data on the cognitive processes in question – by showing which brain regions are activated and which processes occurred during the task. Obviously, this perspective involves a different concept of “understanding”: it suggests that a complete understanding of cognition also requires to link it with results from other disciplines, such as neurobiological experiments in animal research down to biophysical accounts of receptor function. Such neurocognitive theories allow for a “deeper” and more complete explanation of cognitive processes.

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