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This material has been published in

Brain and Cognition

Volume 42, Number 1, February 2000, pp. 113 - 116

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The study of the regenesis of mind in the 21st century

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Running head: Regenesis of mind in the 21st century

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The enigma of consciousness and the brain-mind relationship will - most likely - be unveiled in the 21st century through the new technologies developed at the end of the 20th century and new technologies yet to come. The new technologies will be used to tackle the problem from evolutionary, developmental, normal and pathological brain functioning. A major contribution, however, will surface when investigating a particular perspective of pathological brain functioning - a perspective that has not received any attention in the past: the investigation of the re-emergence of mind out of prolonged coma and coma like states.

Comatose and paracomatose states after severe brain damage

Through recent advances in emergency medicine and intensive care more and more patients survive life threatening conditions such as severe traumatic brain injury, cerebral hypoxia due to cardiac problems, asthmatic status or drowning. With the advent of effective neuroprotective agents and further development of neurosurgery the survival rate of such patients with even more severe brain damage will increase even more. Not only will they survive but an increasing number will recover to a level of normal living. A considerable number, however, will remain in a coma for an extended period of time. Whereas some will pass through coma-like states over weeks, months and sometimes even years before they emerge out of coma, others will continue to live in a conscious state¹ somewhere on a continuum between coma and normal consciousness ranging from vegetative (or apallic) state, akinetic mutism, low awareness state (minimal reactive, minimal conscious state), to locked-in syndrome or states which are not yet identified and labeled. Vegetative state patients, for example, are considered to have normal vegetative, i.e. autonomous functions, but no remaining or recovered cognitive functions. Currently, diagnosis of vegetative state is based on purely clinical investigations of overt behavior observed by the examiner from the „outside“. Covert behavior in vegetative state patients remains clinically inaccessible and the level of their cognitive functioning unclear. To declare these patients „cognitively dead“ and to introduce „cognitive death“ as a diagnostic label does not only lack any scientific basis but is at best not only speculative but also highly unethical. Therefore, these patients pose major practical, scientific, and ethical problems which are intimately interconnected.

¹ These states are labeled here as para-conscious or para-comatous to denote that patients in these states are not unconscious, i.e. comatous, but have some form of altered consciousness without further specification.

Cognitive neuroscience - practical and ethical implications

From a practical and ethical point of view it is a moral obligation for cognitive (neuro-) science to develop techniques to investigate these a-conscious, para-conscious states and mental re-emergence phenomena in the future. Research must establish whether these patients are left with any mental and cognitive capacity, and if so at what level. Detection of preserved or recovering mental and cognitive capacity is critical with respect to medical and economical decision making as in some countries health insurance companies or health services refuse to pay for medical treatment and care after a certain time period of vegetative states. An increasing number of patients is legally withdrawn not only from medication but also from food or are considered as sources for organ transplantation.

Cognitive neuroscience - research implications

From a scientific perspective para-comatose states will offer the unique opportunity to investigate consciousness and other mental functions as emergent phenomena over time from zero functioning in coma to normal functioning in the fully recovered states. The re-emergence of individual functions will allow to identify the mental components, their interdependence and interactions.

The research program will include investigations at the neuroendocrinological, neurophysiological, and behavioral levels and their interactive intersections. Are there hormonal preconditions for mental recovery? For example, does the endogenous rhythmicity of the cortisol system need to be established before any mental functioning reoccurs? Does the rhythmicity of different hormones reoccur at the same time? For example, when cortisol cycles are reestablished do other hormonal cycles such as the sexual hormone cycles in women normalize in parallel? Are the hormonal systems free running or are there regularities, and if so what are the time constants? Does reestablishment of regularities have prognostic value for global recovery? Does hormonal normalization precede or parallel reestablishment of other functional systems? For example, is the sleep-wake cycle coupled with the endocrine cycles, especially the cortisol system or do they run independently? Long term computerized EEG recording can be used to track the reestablishment of sleep-wake cycles from unstable free running wake and sleep phases of varying length. Is reestablishment of a normal sleep-wake cycle a precondition for the return of mental functions? What level of brain activity as indexed by EEG frequency is needed for information processing to evolve? What EEG frequency level is necessary for event related potentials such as the

N100/P200, the P300 or the N400 to occur? Is there an N400 or a P300 when the brain is in a very slow delta range? Or does an N400 only evolve in the alpha stage of recovery? Do these event related potentials reappear in linear succession within and across patients or independently of each other? How are these electrocortical measures related to observable overt behavior? Do they precede such behavior? For example, is there an N400 before the patient shows behavioral indications of language comprehension? Does the development of electrocortical responses bear any relationship to a positive prognosis? What other neurophysiological parameters can be used to track re-emergence of mental functions? Is, for example, chaos analysis of any value?

Similar and other questions can also be investigated by applying imaging techniques such as PET or fMRI. What is the relationship between the emergence of cortical and subcortical functions? Do brainstem functions emerge before cortical functions? Are there distinct re-emergence patterns? For example does activity in the mesencephalic reticular system precede regional cortical activities? Do different behavioral stimuli result in global and undifferentiated activation patterns or in distinct local activation indicating that inhibitory systems have recovered to allow for selective information processing? Is it possible to increase the activity of neuron specific enzymes such as NAA (N-acetyl-aspartate) in relevant brain areas and making it visible using MRI spectroscopy?

At the biochemical level, the dopaminergic, noradrenergic, serotonergic and cholinergic effect of drugs on mental systems needs to be studied. Do these drugs affect different mental systems distinctly or do they only exhibit global effects?

At the behavioral level the circumstances under which patients develop awareness of self, others and the environment have to be studied. When does separation of subject and object occur? At what level of mental functioning do patients recognize themselves, for example, when using a mirror? How does the action system develop? Is there a stepwise development from no action, reflexive re-action, adaptive re-action, through context adequate re-action to spontaneous intrinsically triggered („willed“) actions? How is communication reinstated? For example, do patients modify vegetative/autonomous activities in response to family members versus other persons such as distinct changes in heart rate or breathing rate? Does motor speech develop from rhythmic undifferentiated closing/opening gestures („murmuring“ utterances) into more distinct speech sound patterns?

Finally, with respect to prognosis the validity of various measures has to be investigated, especially whether there is an increase in prognostic power if the findings of several independent measures converge.

Cognitive (neuro-) science has an ethical obligation to develop and provide methodological means to investigate covert cognitive capabilities in paracomatose patients and to establish a scientific and data based foundation for medical decision making in a neuroethical, humanistic framework.