Let's talk about the recovery of motor function following brain damage and the role of amphetamine treatment.

Animal studies (8) and pilot clinical studies (7) have demonstrated that combining amphetamine administration with appropriate motor activity results in sustained improvement in motor function in brain-damaged rats and humans. The effect can be obtained with a single dose of amphetamine. Previously, Luria (12) had summarized a series of human studies from the Soviet Union, most of which related to the early and late treatment of soldiers injured in WWII, that also showed sustained motor function improvement following a single dose of Prostigmin. How the lasting effect can be produced with a single dose is not known.

Amphetamine can induce drug-specific activation of the c-fos gene in the striatum, via activation of the D1 dopamine receptors (11). Fuxe et al. (10) consider it likely that the D1 striatal receptors can activate the c-fos gene by increasing the formation of cAMP. In view of these and other recent findings, we suggest the possibility that the sustained improved motor function may be related to changes in gene expression. Demonstration of such a mechanism would have significant implications for understanding 1) the mechanisms of reorganization of function following brain damage; 2) the role of specific neuroactive substances (including neurotransmitters, neuropeptides and specific neuropharmacological agents to modify them) in the recovery process; and 3) the role of physical and other rehabilitation in the recovery.

The importance of basal the development of neurologic rehabilitation methods on an understanding of neural mechanisms has been discussed elsewhere (1), and a number of possible mechanisms have been examined (6), including those related to the effects of the active participation of the patient in the rehabilitation process on specific neuroactive substances (5).

The possibility that volume transmission (9) may be of importance has recently been evaluated (2, 3, 4). We add here the suggestion that the possible changes in gene expression may relate to synaptic as well as extrapyramidal receptor changes. In the latter case, volume transmission would have to be considered. For example, after a CNS insult, volume transmission may play a role in sustaining the "target" neurons in an active state, to prevent cell death due to de-nervation.

We suggest that it is necessary, at this early stage of development of theory-based neurologic rehabilitation, to speculate on possible relevant mechanisms. Such speculation should lead to experiments, which will in turn lead to more efficient and cost-effective neurologic rehabilitation.

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