Neurochemistry of consciousness: cholinergic pathologies in the human brain

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Publisher Summary

The cholinergic system is implicated in a broad range of disorders of the human brain, including those associated with development (Rett's syndrome, autism, and schizophrenia), and in old age (Alzheimer's and Parkinson's disease, dementia with Lewy bodies (DLB), and progressive supranuclear palsy). Amongst these, autism and DLB are particular examples of brain disorders, which include as central feature disturbances in consciousness. Autism can be considered as a disorder of consciousness. In this disease, there is not generally evidence of reflection and imagination that characterize human consciousness. Of two neurotrophins that control cholinergic neuronal development and maintenance, nerve growth factor (NGF) levels are normal, but brain-derived neurotrophic factor (BDNF) levels are significantly elevated (three-fold) in the basal forebrain in autism. Dementia with Lewy bodies (DLB) is the second most common degenerative dementia in old age, after Alzheimer's disease. In DLB, there are frequent fluctuations in the level of awareness and attention together with persistent visual hallucinations. Neurochemical data indicate an extensive loss of presynaptic cholinergic activity in the cerebral cortex and also reductions in the thalamus and striatum in DLB. Disturbances in consciousness in DLB frequently include fluctuations in the level of awareness and less frequently periodic loss of consciousness. Variations can be detected over very short periods of time, suggesting that fluctuating consciousness arises from dysregulation of continuously active arousal systems.