Medical treatment of amblyopia: Present state and perspectives

Medikamentozno zdravljenje ambliopije

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Abstract

A brief review is provided on the role of experimental modulation of the visual system during its plastic period. The importance of several substances could be demonstrated. Potential clinical applications of available studies for amblyopia treatment are summarised. The role of the dopaminergic system and particularly of dopamine in amblyopia are also discussed. Results of the use of cytidin-5'-diphosphocoline (citicoline) in amblyopia are evaluated in detail. Advantages and indications for a combination of citicoline with part-time occlusion are discussed in detail. Finally, new administration modalities of citicoline, more detailed evaluation of its efficacy and the use of new substances are briefly analysed.

Izvleček

Prikazan je kratek pregled poskusne modulacije vidnega sistema v njegovem plastičnem obdobju. Dokazati je bilo mogoče pomen mnogih snovi. V povzetku so navedene možnosti klinične uporabe razpoložljivih raziskav zdravljenja ambliopije. Prispevek obravnava tudi vlogo dopaminergičnega sistema in predvsem dopamina pri ambliopiji. Podrobno so ocenjeni rezultati uporabe citidin-5'-difosfokolina (citokolina) pri ambliopiji. Podrobno so tudi obravnavane prednosti in indikacije za kombiniranje citokolina s prekrivanjem očesa za določen čas. Na koncu sledi kratka analiza novih načinov aplikacije citokolina, bolj podrobna ocena njegove učinkovitosti ter uporabe novih snovi.

Review

With the visual demands of our society, amblyopia, and particularly unilateral amblyopia, has become a serious socio-economic problem. It is not easy to evaluate the incidence of amblyopia in the entire population, but studies in a particular population subset have underlined an average prevalence of amblyopia of between 1 % and 4 %.[1,2] All forms of amblyopia are characterised by reduced visual acuity, but they differ from one another because of a different prognosis. Amblyopia can occur only during the critical period of development of the visual apparatus. When the same factors that cause amblyopia occur after the visual system has matured, they are not capable of inducing the disease. Therefore, these factors are effective during the first 7–8 years of life; the sooner one of these causes occurs, the more difficult the visual recovery. For this reason, the earlier the therapy is started, the sooner effective results will be obtained.[3] The treatment of amblyopia is based on the interruption of the visual input in the fixing eye, in order to stimulate vision development in the amblyopic eye. However, sometimes this therapeutic approach proves insufficient, owing either to problems of compliance with patching treatment, or to a tendency of losing, over time, the benefits obtained.[4]

For the reasons mentioned above, new treatment modalities for amblyopia are constantly proposed. They include bio-feedback techniques, perceptual training and medical treatment. The latter has been for a long time the dream of strabismologists, ever since the second half of the 19th century. All efforts have been aimed at combining occlusion with active pharmacological stimulation

which could make the therapeutic effect of patching more effective and enduring. Strichnine was proposed initially;[5] in the 50's of the 20th century the use of nicotin acid and oxygen was suggested for suppression and amblyopia.[6] Increasing knowledge has been gathered on the role of neuro-transmitters in the maturation of the visual system. Amblyopic inhibition mechanisms are connected with synaptic neuro-transmission. Beta-blockers as well as norepinephrine can delay the plasticity of the visual system.[7,8] Exogenous nerve growth factor prevents the effect of visual deprivation.[9] Much more evidence has been gathered on this point and brought to a rational use of a neuro-mediator such as dopamine in amblyopia. This substance has been shown to improve temporarily suppression scotomas and visual function in amblyopia.[10] The association of carbodopa-levodopa has been demonstrated to induce longer lasting effects.[11-13] The efficacy of dopamine has been shown objectively by means of functional MRI. Systemic side-effects, however, were present with this type of treatment.

Our Group has been involved in the use of CDP-choline (citicoline) in amblyopia since 1992. Citicoline enhances endogenous dopamine activity and does not induce systemic side-effects. The stimulation of the dopaminergic system with CDP-choline may be attributable to a mechanism that causes an improvement in the retinal and post-retinal performance of glaucomatous patients when treated with CDP-choline.[14] These considerations have suggested a rationale for using CDP-choline in patients suffering from amblyopia,. Inadequate foveal or peripheral retinal stimulation and/or abnormal binocular interaction causing different visual input from the foveae during the critical period of visual development induce an alteration in genetically programmed processes that guide the ganglion axons towards the lateral geniculate body and then to the visual cortex. As this development process is influenced by both endogenous and exogenous stimuli, it could be pharmacologically modulated. Previous studies[15-19] report that intramuscular cytidin-5'-diphosphocholine (also known as CDP-choline or citicoline), enhances the effects of patching in amblyopic patients of different ages. We have shown that this substance improves temporarily visual acuity, visual evoked responses and contrast sensitivity in both eyes of adult patients with amblyopia. It enhances the effect of part-time occlusion in children. A 30-day treatment with 500 mg per day in children produced results which would last 6 months. Treatment was therefore prescribed twice a year. Yet, till recently, citicoline could be administered only intra-muscularly. This made it impossible to prescribe the substance in very young children. An oral preparation of citicoline is now available. Our Group has experienced its efficacy and data appear to confirm the previous observations made with CDP-choline administered via the intramuscular route, which demonstrated that the treatment is a useful complement to patching in order to shorten conventional patching treatment.[20] It is also possible that in the near future we shall be able to modulate the plasticity of the visual cortex, restored by the use of some substances providing pharmacological stimulation.[21,22] It seems already possible to temporarily improve contrast sensitivity in the amblyopic visual cortex by means of repetitive transcranial magnetic stimulation (rTMS), indicating continued plasticity of the amblyopic visual system in adulthood, and so opening the way for a potential new therapeutic approach to the treatment of amblyopia.[23]

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