Glenn Irvine prize awardee

XK is a partner for VPS13A: A molecular link between Chorea Acanthocytosis and McLeod syndrome

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Abstract

Vps13 is a highly conserved lipid transfer protein found at multiple inter-organelle membrane contact sites. In yeast, the single Vps13 protein is recruited to different contact sites through interaction with different adaptor proteins. Mutations in human VPS13A cause the neurodegenerative disease Chorea Acanthocytosis (ChAc). The symptoms of ChAc resemble those of McLeod syndrome caused by mutations in the XK gene. These observations suggest that XK could be a partner protein for VPS13A. We report that XK forms a complex with VPS13A in human cells, and XK overexpression relocalizes VPS13A from lipid droplets to subdomains of endoplasmic reticulum (ER). A VPS13A protein carrying the ChAc-linked mutation (W2460R) in the VPS13 adaptor binding (VAB) domain failed to localize to lipid droplets and did not relocalize to ER subdomains upon XK overexpression. These observations suggest that the function of VAB domain in regulating VPS13 localization might be conserved in human VPS13A and that disruption of a VPS13A-XK complex is the common basis for ChAc and McLeod syndrome.

Focus is on patients, with caregivers present

Impact of Neuroacanthocytosis syndromes on speech and swallowing function

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Abstract

Aim: The aim of the talk was to describe the variability of speech and swallowing presentation in patients with NA syndromes and to discuss treatment options for behavioural therapies.

Background: Speech and communication can be affected at every stage of the disease process, and dysarthria can be one of the earlier symptoms of the disease. Similarly maintaining the safety and pleasure from eating and drinking with family is part of our quality of life.

Methods: A combination of anecdotal evidence from short reports and clinical experience shows the wide spectrum and the changes of presentation, from hyperkinetic (too much movement) to hypokinetic (too little). Symptoms affecting speech involve choreic movements of the trunk and the limbs, oro-facio-lingual dyskinesias, limb or facial dystonias, and difficulty initiating movement, with reduced amplitude. Factors contributing to the variability of presentation are age of onset (young adult or middle aged), other treatments (surgical, BOTOX, pharmacological), effect of stress and fatigue, and availability of multidisciplinary team input.

Results: The aim of any speech and swallowing intervention is to maintain communication and participation for as long as possible. A variety of speech approaches can be deployed, depending on the stage and the particular symptoms. Sensory tricks can help and need to be acknowledged and expanded. Mouth guards can be useful for tongue dystonia but can impair speech. BOTOX and other pharmacological effects should be monitored for their effects on function before and after their initiation. Working on louder voice can improve not just voice, but articulation clarity. Singing is always beneficial for both the voice and the soul. Voice banking and Alternative communication systems will be discussed.

Swallowing can be affected in the oral stage by the uncontrolled movements of the tongue and the reduced lip seal. Pharyngeal stage can preserve the safety of swallowing. Patients should be encouraged to sit more upright if possible and to minimize distractions during meals. Training the expiratory muscles (with e.g. the EMST150) can help with the cough strength and clearing of saliva.

Conclusion: Maintaining communication and swallowing function for as long as possible is paramount. Balancing the hypo-and hyper-kinetic symptoms throughout the disease process requires flexibility and further knowledge, through more longitudinal studies.