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Is autism due to brain desynchronization?

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Abstract

The hypothesis is presented that a disruption in brain synchronization contributes to autism by destroying the coherence of brain rhythms and slowing overall cognitive processing speed. Particular focus is on the inferior olive, a precerebellar structure that is reliably disrupted in autism and which normally generates a coherent 5–13 Hz rhythmic output. New electrophysiological data reveal that the continuity of the rhythmical oscillation in membrane potential generated by inferior olive neurons requires the formation of neuronal assemblies by the connexin36 protein that mediates electrical synapses and promotes neuronal synchrony. An experiment with classical eyeblink conditioning is presented to demonstrate that the inferior olive is necessary to learn about sequences of stimuli presented at intervals in the range of 250–500 ms, but not at 700 ms, revealing that a disruption of the inferior olive slows stimulus processing speed on the time scale that is lost in autistic children. A model is presented in which the voltage oscillation generated by populations of electrically synchronized inferior olivary neurons permits the utilization of sequences of stimuli given at, or faster than, 2 per second. It is expected that the disturbance in inferior olive structure in autism disrupts the ability of inferior olive neurons to become electrically synchronized and to generate coherent rhythmic output, thereby impairing the ability to use rapid sequences of cues for the development of normal language skill. Future directions to test the hypothesis are presented.

Section snippets

Basic anatomy and physiology

The IO is a most remarkable structure, most simply because it comprises one-third the volume of the human medulla oblongata (Fig. 1a). The IO is the starting point of the olivocerebellar system, which consists of IO neurons in the ventral medulla, Purkinje cells in the cerebellar cortex, and deep cerebellar nuclear neurons (DCNNs) embedded in the subcortical white matter (Fig. 1b). From a physiological view, the IO is even more remarkable because it contains the highest density of electrical…

The IO is necessary for processing short time intervals: a parallel to autism

Our recent experiments have shown that IO-deficient rats are impaired in their ability to process rapid sequences of stimuli at a time scale that is closely identical to the perceptual slowing of autistic children. We have used classical conditioning of the eyeblink reflex to examine the effect of removing the IO on the computational speed of the brain. In classical eyeblink conditioning, an eyeblink is acquired to a conditioned stimulus (CS) when the CS is presented in temporal contiguity with …

Genetic deconstruction of electrical coupling: effects on neuronal oscillation in the IO and implications for autism

Is there a role for IO synchrony and rhythmicity in facilitating the speed of stimulus processing? Neuronal modeling has consistently suggested that electrical synapses are necessary for the strength of 10Hz and 40Hz electrical oscillations in the IO and neocortex, respectively (Manor et al., 1997, Traub et al., 2001). This view was confirmed for the fast neocortical oscillation, when embryonic deletion of the gene that codes for the protein that forms electrical synapses, connexin36, abolished …

IO malformation: a common neuropathology of SIDS, dyslexia, and autism

From a broader perspective, it is important to note that two other neurological syndromes have been correlated with alterations in the cellular organization of the IO: sudden infant death syndrome (SIDS) and dyslexia. A highly quantitative analysis of the IO in 29 cases of SIDS indicated a significant decrease in the packing density and number of IO neurons relative to age-matched controls (Kinney et al., 2002). One current view of SIDS is that developmental abnormalities of the neural…

Future directions with a view toward autism

The previous synthesis lends itself to firm predictions that can be tested in human autistic tissue at the cellular and neuronal network levels of analysis. Future experiments should take advantage of recent advances in subcellular imaging that can be used to answer the following questions. How is the dendritic morphology of IO neurons changed in the autistic brain? Are the spatial interactions between dendritic arbors altered in the autistic IO? Might there be foci of hypercoupling within the…

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Is there a generalized timing impairment in Autism Spectrum Disorders across time scales and paradigms?

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> ...Furthermore, both clinical reports and research literature suggest that the primary diagnostic characteristics of ASD are commonly accompanied by secondary difficulties, such as atypical motor (Ming et al., 2007) and sensory (Blake et al., 2003; Milne et al., 2002) processing. Among such secondary characteristics, difficulties in timing might be a key part of the autistic cognitive profile (e.g., Allman et al., 2011; Bebko et al., 2006; Boucher et al., 2007; Brodeur et al., 2014; Falter et al., 2012a, 2012b, 2013; Gepner and Féron, 2009; Gowen and Miall, 2005; Karaminis et al., 2016; Kargas et al., 2015; Kwakye et al., 2011; Maister and Plaisted-Grant, 2011; Martin et al., 2010; Szelag et al., 2004; Whiting and Dixon, 2015; Ribeiro Zukauskas et al., 2009; for review and clinical discussion, see Allman and Falter, 2015; Boucher, 2001; Falter and Noreika, 2014; Stevenson et al., 2016; Welsh et al., 2005). However, timing deficits in ASD are not unequivocal (e.g., Bebko et al., 2006; Gil et al., 2012; Glazebrook et al., 2008; Jones et al., 2009, 2017; Kwakye et al., 2011; Mostofsky et al., 2000; Wallace and Happé, 2008)....

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