Errata

The pathogenesis of autism in relation to maternal antibodies: from molecule to connectome

Patogenéza autismu vo vzťahu k materským protilátkam: od molekuly až po konektom

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Titulná strana

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Obsah a číslovanie capitol

Contents

Doplnenie zoznamu skratiek

BBB – blood-brain barrier

HC – hippocampus

HSP 70/90 – heat shock protein 70/90

ICD-10 - International Statistical Classification of Diseases and Related Health Problems

IgG – immunoglobulins of the G subclass

MAP2 - microtubule-associated protein 2

MAU - maternal autoantibodies specific of autism

PSD-95 – postsynaptic density 95 protein

RG – radial glial cells

Oprava citácii

Str. 1

While some studies have found over-connected neural systems *(Belmonte & Yurgelun-Todd, 2003*) other studies demonstrated deficit in connections between multiple areas in the brain *(Just et al., 2004)* .

Str. 2

The difference between them is the onset time of symptoms and the amount of them presented *(World Health Institution, 2016, accessed 11.7.2019)*.

Str. 3

. The results have been inconsistent, but largely agree that patients with autism have a high local connectivity and low long-range one. It is believed that the decreased long-range connectivity limits effective information integration between multiple brain areas of both hemispheres which is essential for higher cognitive functions. What are the exact mechanisms responsible for abnormal axonal connectivity remains an enigma. We can speculate that abnormal connectivity may be a consequence of a pathological process that interfere with axonal growth, sprouting and pruning during brain development. The presence of maternal anti-bodies against the fetal brain during pregnancy can represents one of the pathological processes. (reviewed in Belmonte, 2004)

Str. 5

Specific autoimmune diseases that have shown a correlation with autism include: eczema/psoriasis, rheumatoid arthritis, hypothyroidism, type 1 diabetes and systemic lupus erythematosus *(Atladóttir et al., 2009; Chen et al., 2016; Vinet et al., 2015; Wu et al., 2015)*.

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One of the first studies to connect maternal antibodies with autism was done by Warren et al. in 1990. In a sample of 11 children with ASD, their siblings and 20 controls they have

found significantly higher reactivity of peripheral maternal blood against lymphocytes of the autistic children (Warren et al.,1990).

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The IgG-ASD primates have exhibited differences in social behaviour and males have had an enlarged brain volume with biggest difference being in the white matter in the frontal lobes *(Bauman et al., 2013)*.

Str. 11

Thanks to spectrometry peptide sequencing, the proteins corresponding to the identified bands 37-,39-, and 73-kDa were identified as: cypin, stress-induced phosphoprotein 1 (STIP1), collapsin response mediator proteins 1 & 2 (CRMP1 & 2), lactate dehydrogenase A & B (LHD), and Y-box-binding protein (YBX-1). Reactivity to a combination of specific antigens was shown in 23% mothers of children with ASD as opposed to 1% in control group. *(Braunschweig et al., 2013)*.

Mice injected with a series of peptide epitope sequences of LDH, STIP1 and CRMP1 have demonstrated stereotypical self-grooming behaviour, avoiding social interactions with failure at reciprocating juvenile play with peers *(Bauman et al., 2018).*

This has been shown by knock-out model in which cypin mRNA was prevented from maturation using mutated U1 small nuclear RNA (snRNA). The neurons that had this mutant snRNA indicated small or non-existent levels of cypin and fewer dendrites than normal. (Akum et al., 2004)

Str. 12

If cypin expression is inhibited, there is a decrease in dendrite number of hippocampal neurons *(Chen & Firestein, 2007)*.

Str. 14

Figure 5 – (taken from Ariza et al.,2017)

Str. 15

Mitochondrial dysfunction has been linked to ASD by several studies (Frye & Rossignol, 2011; Goh et al., 2014; Weissman et al., 2008).

Connectivity is a major organizing principle of the nervous system and conceptualizing the brain as a network (the ‘connectome’) represents fundamental and innovative framework for understanding clinical brain disorders (Bullmore & Sporns., 2009).

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Hub damage will have a disproportionate impact on the network’s global efficiency of information processing; and thus be more likely to result to clinical symptoms such as

impairment of cognitive functions, that depend on integrative network processes (Honey & Sporns., 2008).

Connectivity in ASD has been discussed for a long time. Some people have argued that there is a surfeit of connectivity (Rubenstein & Merzenich., 2003), while other studies have shown examples of underconnectivity (Jakab et al., 2013). It seems as though both sides of the argument are right, high-local connectivity with a lot of cross-talk has emerged from abnormal neuronal and synaptic development and thereby causing hyper-arousal and potentially causing a weak central coherence – decreased long-range connectivity (Belmonte & Yurgelun-Todd, 2003).

Str. 17

This alternation has caused loss of social memory, indicating that these neurons have a role in sociocoginitive memory processing which has also one of the areas ASD patients differ to controls. (Hitti & Siegelbaum, 2014)

Str. 18

They form during development with at first slow dendrite growth, rapid period of dendritic extension and then a period of stabilization of dendritic arbour (Williams & Truman, 2004).

Various dendrite number abnormalities have been reported in patients with ASD (Hutsler & Zhang, 2010; Mukaetova-Ladinska et al., 2004), which correlates with the fact that cypin and CRMP have functions that modify it and therefore they can be associated with this pathological observation.

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(Frye & Rossignol,2011)

(Lopes et al.,2005)

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