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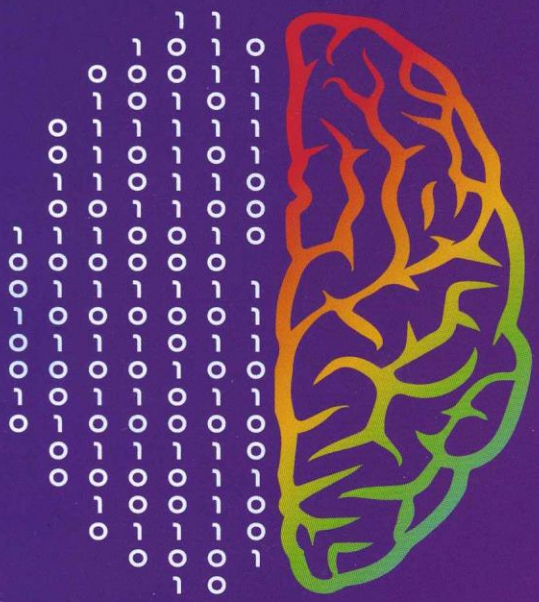

ORGANIZATORI

Razred za medicinske znanosti HAZU (Odbor za neuroznanost i bolesti mozga)
Međunarodni institut za zdravlje mozga
Znanstveni centar izvrsnosti za temeljnu, kliničku i translacijsku neuroznanost
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TAU I LAKI PROTEINI NEUROFILAMENATA KAO BIOLOŠKI BILJEZI PERINATALNE ENCEFALOPATIJE

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Dijagnoza hipoksično-ishemičke encefalopatije u novorođenčadi trenutno se temelji na kliničkim simptomima, slikovnom prikazu te elektrofiziološkom praćenju (Graham et al., Curr Opin Pediatr, 2018, u tisku). Biokemijska procjena nedostatka kisika u fetusa (asfiksije) tradicionalno se provodi određivanjem plinova analizom venske krvi iz umbilikalne arterije pri porođaju, no taj podatak ne govori puno o stupnju oštećenja mozga. Nažalost, ni slikovni prikaz magnetskom rezonancijom (MRI) nije osjetljiva metoda za ranu vizualizaciju hipoksičnog oštećenja. Osim toga, zbog snimanja MR se dojenčad mora premještati iz jedinice intenzivne njege. Navedene prepreke možda bi se mogle premostiti upotrebom dupleks sonografije kroz veliku fontanelu, ali ultrazvuk glave kao slikovni biomarker ima relativno nisku osjetljivost i nije općeprihvaćen (Bano et al., J Pediatr Neurosci, 2017). U jedinicama intenzivne njege novorođenčadi sve se češće prati regionalna saturacija cerebralne krvi kisikom ($rScO_2$) pomoću bliske infracrvene spektroskopije, iako ta metoda mjerenja ima ograničenu penetraciju od 1-2 cm i nije dovoljno potvrđena.

Hipotermija je trenutno jedini standardni postupak za sprječavanje trajne neurološke onesposobljenosti novorođenčadi s umjerenom do teškom perinatalnom hipoksično-ishemičkom encefalopatijom, no usprkos liječenju gotovo polovica takve novorođenčadi ima loš ishod (Shankaran i sur., N Engl J Med 2012.). Liječenje encefalopatije u novorođenčadi otežano je prvenstveno nedostatkom mjerljivih bioloških biljega koji bi odražavali stupanj oštećenja, pomogli u izradi optimalnog plana liječenja te služili za davanje prognoze. U potrazi za točnim, ranim prediktivnim biljezima asfiksije u fetusa koji bi kliničare upućivali kada je potrebno neuroprotektivno liječenje, iz krvi pupkovine desetoro novorođenčadi s umjerenom do teškom intrapartalnom asfiksijom i 18 zdrave novorođenčadi izmjerene su u pupčanoj krvi koncentracije tau proteina i lakih proteina neurofilamenata (Toorell i sur., J Matern Fetal Neonatal Med, 2017, elektroničko izdanje članka objavljeno prije pisanog). Razine tau i lakih proteina neurofilamenata bile

su znatno veće nakon asfiksije i korelirale su s težinom neuroloških deficita. Ti su rezultati ohrabrujući, ali su za procjenu vrijednosti mjerenja tau proteina i lakih proteina neurofilamenata u krvi potrebne dodatne studije na većem broju novorođenčadi prije uvođenja u kliničku praksu.

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TAU AND NEUROFILAMENT LIGHT PROTEINS AS BIOMARKERS FOR PERINATAL ENCEPHALOPATHY

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The diagnosis of hypoxic-ischemic encephalopathy in neonates is currently based on clinical symptoms, imaging, and electrophysiological monitoring (Graham et al., Curr Opin Pediatr, 2018, in press). Biochemical evaluation of fetal oxygen deprivation (asphyxia) has been traditionally performed using umbilical arterial blood gases at birth, but this test is poorly predictive of injury. Unfortunately, magnetic resonance imaging (MRI) biomarkers also lack early sensitivity for hypoxic injury. Additionally, MRI requires the infant to be moved from the intensive care unit. These hurdles may be eventually overcome with the use of transfontanellar duplex brain ultrasonography, but head ultrasound as an imaging biomarker has relatively low sensitivity and is not universally accepted (Bano et al., J Pediatr Neurosci, 2017). In neonatal intensive care units, the regional cerebral tissue oxygen saturation (rScO2) is increasingly being monitored by near-infrared spectroscopy (NIRS), although this method has a limited penetration depth of 1-2 cm and has not been sufficiently validated.

To prevent life-long neurological disabilities in neonates with moderate-to-severe perinatal hypoxic-ischemic encephalopathy, hypothermia is currently the only standard treatment, but almost half of those neonates have abnormal outcomes despite treatment (Shankaran et al., N Engl J Med 2012). Treatment of neonatal encephalopathy is impeded mainly by the lack of quantifiable biomarkers that could measure the degree of injury, assist in making an optimal treatment protocol, and yield prognostic information. In search for accurate, early predictive markers of fetal asphyxia to direct the clinician as to when to provide neuroprotective therapy, neuronal tau and neurofilament light proteins have been analyzed in the umbilical blood of ten cases of severe-moderate intrapartum asphyxia and in 18 control cases (Toorell et al., J Matern Fetal Neonatal Med, 2017, epub ahead of print). The levels of both tau and neurofilament proteins were significantly higher after asphyxia and correlated with the severity of the neurological deficits. These results are encouraging, but additional studies are

needed to assess further the value of blood tau and neurofilament protein levels in clinical practice.

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