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Abstracts

Articles appearing in the January 2021 issue

Placental Transfer of NMDAR Antibodies Causes Reversible Alterations in Mice

Objective To determine whether maternofetal transfer of NMDA receptor (NMDAR) antibodies has pathogenic effects on the fetus and offspring, we developed a model of placental transfer of antibodies.

Methods Pregnant C57BL/6J mice were administered via tail vein patients' or controls' immunoglobulin G (IgG) on days 14–16 of gestation, when the placenta is able to transport IgG and the immature fetal blood-brain barrier is less restrictive to IgG crossing. Immunohistochemical and DiOlistic (gene gun delivery of fluorescent dye) staining, confocal microscopy, standardized developmental and behavioral tasks, and hippocampal long-term potentiation were used to determine the antibody effects.

Results In brains of fetuses, patients' IgG, but not controls' IgG, bound to NMDAR, causing a decrease in NMDAR clusters and cortical plate thickness. No increase in neonatal mortality was observed, but offspring exposed in utero to patients' IgG had reduced levels of cell-surface and synaptic NMDAR, increased dendritic arborization, decreased density of mature (mushroom-shaped) spines, microglial activation, and thinning of brain cortical layers II–IV with cellular compaction. These animals also had a delay in innate reflexes and eye opening and during follow-up showed depressive-like behavior, deficits in nest building, poor motor coordination, and impaired social-spatial memory and hippocampal plasticity. Remarkably, all these paradigms progressively improved (becoming similar to those of controls) during follow-up until adulthood.

Conclusions In this model, placental transfer of patients' NMDAR antibodies caused severe but reversible synaptic and neurodevelopmental alterations. Reversible antibody effects may contribute to the infrequent and limited number of complications described in children of patients who develop anti-NMDAR encephalitis during pregnancy.

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Anti-CD20 Therapies and Pregnancy in Neuroimmunologic Disorders: A Cohort Study From Germany

Objective To report pregnancy outcomes and disease activity (DA) in women with MS, neuromyelitis optica spectrum disorders (NMOSDs), and other neuroimmunologic diseases (ONID) after treatment with rituximab (RTX)/ocrelizumab (OCR) 12 months before or during pregnancy.

Methods Data were collected in the German MS and pregnancy registry and centers from the Neuromyelitis Optica Study Group. Sixty-eight known outcomes of 88 pregnancies from 81 women (64 MS, 10 NMOSD, and 7 ONID) were included and stratified in 3 exposure groups: >6M-group = RTX/OCR >6 but ≤12 months before the last menstrual period (LMP) (n = 8); <6M group = RTX/OCR <6 months before the LMP (n = 47); preg group = RTX/OCR after the LMP (n = 13).

Results Pregnancy outcomes were similar between groups, but significantly more preterm births (9.8% vs 45%) occurred after exposure during pregnancy. Overall, 2 major congenital abnormalities (3.3%), both in the preg group, were observed. Three women had severe infections during pregnancy. All women with MS (35) and 12/13 women with NMOSD, RTX/OCR exposure before the LMP and known pregnancy outcomes after gestational week 22 were relapse free during pregnancy. Five of 29 (17.2%) women with relapsing-remitting MS (RRMS) and 1 of 12 (8.3%) with NMOSD and at least 6 months postpartum follow-up experienced a relapse postpartum. Duration of RTX/OCR and early retreatment but not detection of B-cells were possible predictors for postpartum relapses in patients with RRMS/NMOSD.

Conclusions Although RTX/OCR might be an interesting option for women with RRMS/NMOSD who plan to become pregnant to control DA, more data on pregnancy outcomes and rare risks are needed.

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M. Bodro, Y. Compta, R. Sánchez-Valle. 2020;8:e923. doi.org/10.1212/NXI.0000000000000923

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COVID-19 and MS disease-modifying therapies

J.R. Berger, R. Brandstadter, A. Bar-Or. 2020;7:e761. doi.org/10.1212/NXI.0000000000000761

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