NEWS

Community Newsletter: Maternal immune activation, mitochondria and synaptogenesis, attentional set-shifting

BY **CHELSEY B. COOMBS**

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Hello, and welcome to the Community Newsletter! I'm your host, **Chelsey B. Coombs**, *Spectrum*'s engagement editor.

The first study we're looking at this week is from *Nature Neuroscience*: "**Rescue of maternal immune activation-induced behavioral abnormalities in adult mouse offspring by pathogen-activated maternal Treg cells**."

> Reversal of **#autism**-relevant behaviors and abnormal brain microstructure in male offspring of mice that experienced maternal immune activation (MIA) by pathogen-activated maternal Treg cells**https://t.co/mrVAKvCdCj**
>
> — Nature Neuroscience (@NatureNeuro) **April 15, 2021**

In the study, the researchers used an antigen from the parasite *Toxoplasma gondii* to cause maternal immune activation (MIA) in mice. Male offspring exhibited more marble burying —considered by some to be an analog to repetitive behaviors in autistic people — than wildtype mice, along with atypical brain microstructure and immune system dysregulation. However, the researchers were able to reverse those changes using an infusion of activated regulatory T cells.

"To our knowledge, [this] is the first investigation on adoptive immune cell transfer therapy to treat behavioral abnormalities induced by MIA," the researchers wrote.

Roser Nadal, associate professor at the Universitat Autònoma de Barcelona in Barcelona, Spain, called the research “promising.”

> Promising! Via **@elenagalea1** **https://t.co/H824gT0wcF**
>
> — Roser Nadal (@RoserNadal) **April 15, 2021**

However, many, like **Alexander Arguello**, program officer at the National Institute of Mental Health in Bethesda, Maryland, disagreed with the researchers’ characterization of a mouse burying a marble as an example of an autism-like behavior.

> if burying a marble is "autism-relevant," i'm curious as to what is autism-irrelevant... **https://t.co/PDK83HeMhH**
>
> — Alexander Arguello (@NeuroMinded) **April 15, 2021**

Nicola Grissom, assistant professor at the University of Minnesota in Minneapolis and Saint Paul, Minnesota, wrote, “Sometimes people outside the field don't believe me when I start ranting about marble burying and the weird circular logic of using it to show a mouse is an ‘autism model.’”

> Sometimes people outside the field don't believe me when I start ranting about marble burying and the weird circular logic of using it to show a mouse is an "autism model". They think I'm complaining about something that no one does anymore. I wish I was! **https://t.co/E19ESspSgq**
>
> — Grissom Lab (@NicolaGrissom) **April 19, 2021**

The next tweet comes from Paola Bezzi, principal investigator at the University of Lausanne in Switzerland, whose new research paper, “**Mitochondrial biogenesis in developing astrocytes regulates astrocyte maturation and synapse formation**,” was published in *Cell Reports*.

> Mitochondrial biogenesis in developing astrocytes regulates astrocyte maturation and synapse formation **https://t.co/emnYiQWQSw** Congrats **@Zehndy @francescopetre2 @Eva_DOF @Mirko_Santello @Jen_Romanos** ! **@unil @DNF_neuro @DipFisioFarm @SapienzaRoma**
>
> — paola bezzi (@pbezzi69) **April 14, 2021**

The researchers did a number of in vivo and in vitro experiments using mice to show that the creation of mitochondria in astrocytes is necessary for synaptogenesis, the formation of synapses between neurons. They also found that the process depends on the upregulation of a co-activator of a metabolic regulator called PGC-1?.

“Our findings show that the developmental enhancement of mitochondrial biogenesis in astrocytes is a critical mechanism controlling astrocyte maturation and supporting synaptogenesis, thus suggesting that astrocytic mitochondria may be a therapeutic target in the case of neurodevelopmental and psychiatric disorders characterized by impaired synaptogenesis,” the researchers wrote.

Manuel Mameli, associate professor at the University of Lausanne, tweeted, “A variety of approaches defining the relevance of mitochondrial function in defining the steps through which astrocytes and synaptic function mature. Must read!”

> This is an outstanding piece of work. A variety of approaches defining the relevance of mitochondrial function in defining the steps through which astrocytes and synaptic function mature. Must read! **https://t.co/AdkBk51UwD**
>
> — Manuel Mameli (@_mameli_) **April 14, 2021**

João F Oliveira, principal investigator at the University of Minho in Minho, Portugal, tweeted that it was “a wonderful study, beautiful images!”

> A wonderful study, beautiful images! Congratulations **@pbezzi69 @Zehndy**

> **@Mirko_Santello https://t.co/DzDM3EHhEm**
>
> — João F Oliveira (@Joao_F_Oliveira) **April 16, 2021**

Alfonso Oyarzábal Sanz, postdoctoral researcher at the Institut de Recerca Sant Joan de Déu in Barcelona, Spain, wrote that "these interesting results will also be key on the understanding of several pathologies and on the development of targeted drug and metabolic therapies."

> Such a beautiful paper! Mitochondria in developing astrocytes as regulators of synapse formation. These interesting results will also be key on the understanding of several pathologies and on the development of targeted drug and metabolic therapies. **https://t.co/o3yxkqkkSU**
>
> — Alfonso Oyarzábal Sanz (@OyarzabalSanz) **April 14, 2021**

Our last thread this week comes from **Timothy Spellman**, instructor at Weill Cornell Medicine in New York City, who summarized his new paper in *Cell*, "**Prefrontal deep projection neurons enable cognitive flexibility via persistent feedback monitoring**."

> Very pleased to share our latest, out today in **@CellCellPress**.**https://t.co/va2b6L8gj6**
>
> We looked at the role of prefrontal neurons in a rodent model of cross-sensory attention shifting, and get this...
>
> — Timothy Spellman (@TimJSpellman) **April 15, 2021**

The study looks at the neuroscience behind attentional set-shifting, which occurs when a person shifts her attention to ignore a previously relevant stimulus and pay attention to a previously irrelevant stimulus. This type of cognitive flexibility has been shown to be more **difficult for some autistic people**.

The researchers used a mouse model of attentional set-shifting along with optogenetics and twophoton calcium imaging to determine how prefrontal cortex (PFC) neurons affect attention shifting.

“Rather than modulating attention in real time, PFC output neurons serve to integrate and maintain representations of recent behaviors and their consequences,” the researchers wrote. In a tweet, Spellman compared this to working memory.

> Instead, here it acts as a feedback monitor, tracking success on recent trials to direct attention on upcoming trials. Sort of like working memory :)
>
> — Timothy Spellman (@TimJSpellman) **April 15, 2021**

Spellman tweeted that the second major finding was that “projection neurons’ task involvement formed a topological gradient, with cells in deeper layers representing more task information, regardless of their projection target.”

> Instead, we found that projection neurons’ task involvement formed a topological gradient, with cells in deeper layers representing more task information, regardless of their projection target.
>
> — Timothy Spellman (@TimJSpellman) **April 15, 2021**

Luiz Pessoa, professor at the University of Maryland in College Park, Maryland, responded, “The era of understanding cortical-subcortical loops might not be too far!”

> The era of understanding cortical-subcortical loops might not be too far! **https://t.co/FeH3p4Cc6N**
>
> — Luiz Pessoa (@PessoaBrain) **April 15, 2021**

Abhi Banerjee, senior lecturer at Newcastle University in the United Kingdom, tweeted, “Nice to see something we thought deeply about as well. Well done authors.”

> PFC neurons enable crossmodal set-shifting by tracking recent trial outcomes and via persistent feedback monitoring. Representations of trial feedback form a topological gradient. Nice to see something we thought deeply about as well. Well done authors.. ???????? **https://t.co/pA8MuVFfDn**
>
> — Abhi Banerjee (@abhii_mit) **April 16, 2021**

Puja Parekh, postdoctoral researcher at Weill Cornell Medical College, called it a “tour de force” that included “some surprising findings about how PFC facilitates rule switching by feedback monitoring.”

> Tour-de-force new work from **@TimJSpellman** **@MalkaSvei** Jesse Kaminsky **@GabaManzano** and Conor Liston out in Cell ????. Some surprising findings about how PFC facilitates rule switching by feedback monitoring. Congrats team! **https://t.co/FSLkAIvPgv**
>
> — Puja Parekh, Ph.D. (@_DrOctothorpe_) **April 15, 2021**

That’s it for this week’s edition of *Spectrum*’s Community Newsletter. If you have any suggestions for interesting social posts you saw in the autism research sphere this week, feel free to send an email to me at chelsey@spectrumnews.org. See you next week!