How very low birth weight affects brain development

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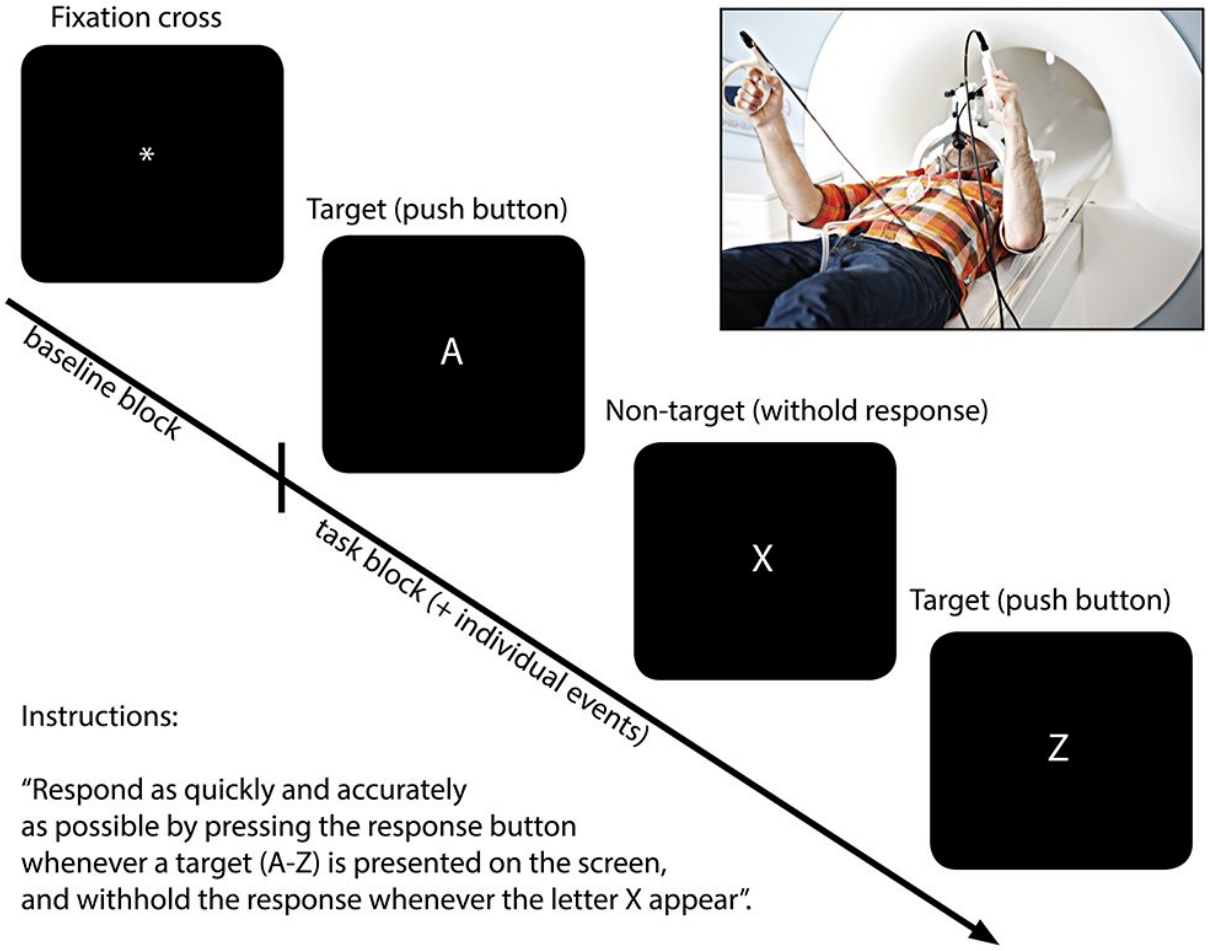


Study participants were told to press a button when they saw a letter in their video goggles, except when the letter was X. This task enabled researchers to see which parts of the participants' brains were engaged when they did the task. Credit: Alexander Olsen/*NeuroImage*

Every year, one in 10 babies worldwide are born too early. That's roughly 15 million children, according to the World Health Organization. When children are born too soon, they are at higher risk of mental and physical disabilities, especially if they weigh less than 1500 grams at birth.

While three-quarters of these preterm births are thought to be preventable, sometimes it's simply not possible. This has researchers like Alexander Olsen, an associate professor at the Norwegian University of Science and Technology (NTNU), working to better understand the consequences of very low birth weights on cognitive development. While Olsen's primary research interest is traumatic brain injury, his research using fMRI on this topic attracted the attention of colleagues in Trondheim who had been working with very low birth weight individuals and brain development.

He worked closely with the head of the Trondheim fMRI Group, Asta Håberg, to expand his research to include a collaboration with the Centre for Early Brain Development, which is conducting a long-term study of individuals with low birth weight. The collaboration also grew to include researchers from the University of Southern California's Imaging Genetics Center at the Stevens Institute for Neuroimaging and Informatics.

"The idea emerged that a lot could potentially be learned through studying these groups in parallel, because they are both typically characterized by alterations in the white matter of the brain, although for different reasons," he said. White matter is important because it provides connectivity between different areas of the brain.

"Comparing how brain function adapts differently to pre- and perinatal injuries and those acquired as adults could provide important information on how the brain works in general," he added.

Cognitive control a problem

Olsen and his colleagues wanted to see how the brains of very low birth weight individuals differed from their normal birth weight cohorts when it came to cognitive control, and the ability to think proactively or reactively about different tasks. That's because cognitive control dysfunction is one of the biggest problems facing very low birth weight individuals, Olsen said.

Chief Radiographer Bjarte Snekvik and Associate Professor Alexander Olsen from the Norwegian University of Science and Technology (NTNU) illustrate how study subjects perform the fMRI task (the person in the photo was not a study participant). Study participants used specially designed response buttons (as shown) and could view the task through video goggles. Credit: Geir Mogen, NTNU

"Cognitive control is related to the goal-directed regulation of thoughts, actions and emotions," Olsen said. "You have to effectively organize and quickly use your mental capacities in a flexible way to cope with the world. A lot of individuals born with very low birth weight have problems with that."

To study this question, the researchers studied a group of very low birth weight individuals who were born between 1986 and 1988 in Trondheim, Norway. These individuals had already participated in MRI studies in Trondheim when they were one, five, 14 and 20 years old. Thirty-two individuals between 22 and 24 years of age from this group participated in Olsen's study and were matched with same-aged controls that had normal birth weights.

For the first time in this cohort, the researchers used fMRI imagery to conduct their work, which allows them to see activation in different parts of the brain as study subjects are engaged in a task. In this study, participants looked at a computer screen while in the scanner and were shown a series of random letters. Their task was to press a button as quickly as possible when they saw a new letter pop up on the computer screen, except when the letter was "x." The most common response was to press the button, because the letter "x" was only presented 10 percent of the time.

"You need two different types of cognitive control to complete this assignment," Olsen said. "So that simple task gave us a lot of information."

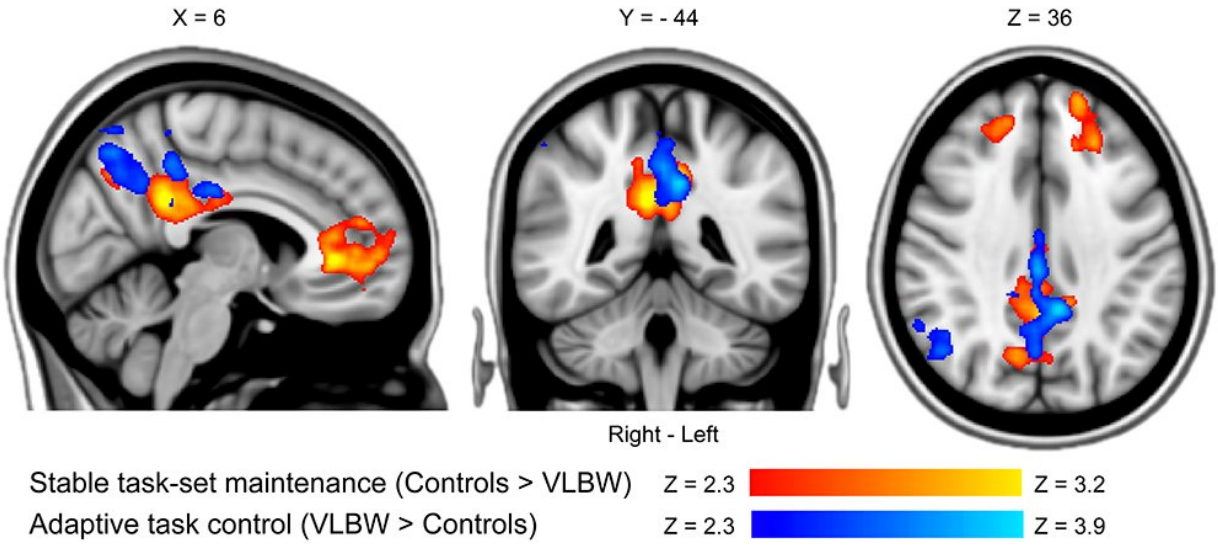
Proactive and reactive systems

The brain is constantly working to create meaning out of the flood of information, Olsen says. Researchers have identified two processes the brain relies on to achieve this task: a proactive cognitive control

function, and a reactive function. Proactive cognitive control relates to proactively working on a task—like the task given to study participants in the MRI scanner. They knew that most of the time, they had to press the button, and they mentally prepared, in a proactive way, to identify new letters as each letter popped up, and to find a balance so that they could respond as quickly and accurate as possible.

But the appearance of the "x" on the screen required a different reaction, Olsen said. "The reactive system kicks in when something happens that is not expected," he said. "Then you need to adapt your behaviour and react to the new information. You have to throw away your old plan and come up with a new plan."

The difference between the two different cognitive systems turned out to be important in explaining other behavior in the very low birth weight individuals, the researchers found.



The orange-yellow areas show where low birth weight individuals had less proactive cognitive control (Stable Task-Set Maintenance) activation in the brain. The blue/light blue areas show where they had more reactive cognitive

control (Adaptive Task Control) activation, compared to the normal birth weight control group. Credit: Alexander Olsen/*NeuroImage*

More reactive, less proactive

The very low birth weight study participants completed the tasks as well as the normal birth weight participants, the researchers found. But they used different cognitive functions to do so, Olsen said.

"What we found was that the preterm group had less proactive brain activation and were more reactive compared to the normal birth weight control group," Olsen said.

This hyper-reactive brain activation signature was accompanied with poorer white matter organization in the brain, and was associated with lower fluid intelligence and anxiety problems. Researchers define fluid intelligence as the ability to think abstractly, identify relationships and solve novel problems.

This difference meant "their brains reacted as if they were encountering something new each time," he said. "It suggests their brains are hypervigilant due to suboptimal organization of the central nervous system. One interpretation is that they are less prepared and more surprised each time, which might create more anxiety problems."

Making sense of anxiety

As both a researcher and a clinical neuropsychologist, Olsen thinks about the potential applications of his research findings.

"As a clinician, this is particularly interesting," he said. "It makes sense

as to why, when you meet some of these individuals as patients, they are experiencing problems with cognitive control function, and having this tied to other emotional problems."

Although the fMRI isn't a practical tool for a clinical setting, the researchers' findings can provide a backdrop for better understanding patients in this group, he said.

"When we work with people with cognitive dysfunction or anxiety problems, we are trying to help them be more proactive in how they prepare for certain situations, so they don't have to rely on reactive problem solving as much," Olsen said. "When you work with cognitive behavioral therapy or cognitive rehabilitation, you work on getting structure into people's lives so they don't have to rely too much on their online cognitive control processing. Creating structure and routine in your life frees up cognitive control resources that can instead be more effectively used for dealing with those things that can't be planned for."

More information: Alexander Olsen et al, Preterm birth leads to hyper-reactive cognitive control processing and poor white matter organization in adulthood, *NeuroImage* (2017). DOI: 10.1016/j.neuroimage.2017.11.055

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