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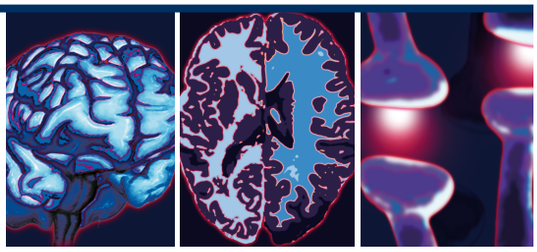


Infants that later develop autism show differences in early brain development

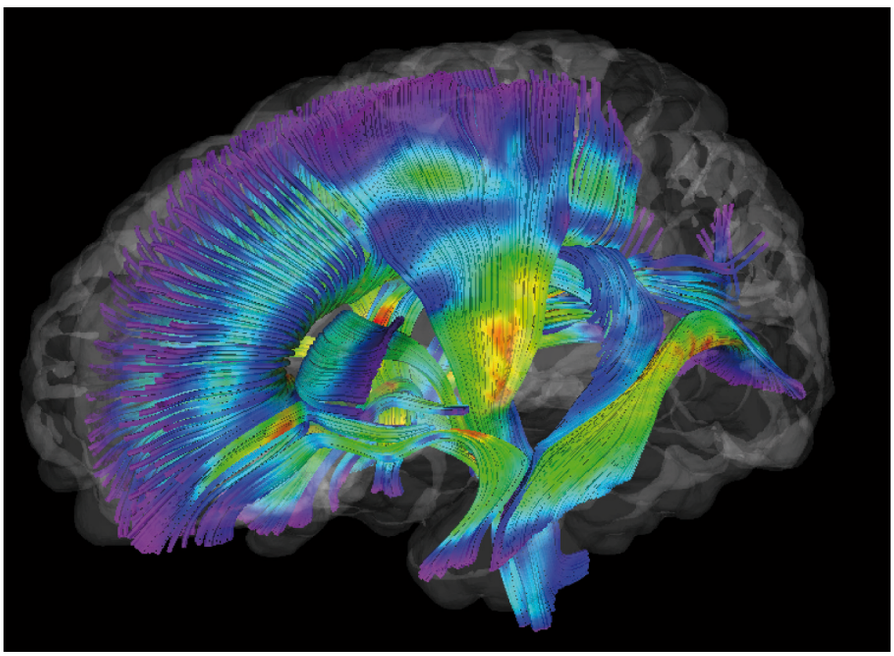
Brain imaging in infants that later develop autism has demonstrated differences in development between autistic and nonautistic children.

Research, led by the University of North Carolina (NC, USA), has shown that developmental differences in the brains of infants occur before autism symptoms first appear, by imaging the brains of 6-month-old infants thought to be at a high risk of developing autism.

There are two important implications from this study; differences in brain development were found before typical behavioral symptoms of autism are observed and these differences occurred throughout the brain, further evidence for the theory that autism does not affect just one location in the brain.

Joe Piven from the University of North Carolina, one of the authors of the study, said to *Neuropsychiatry* that their research has shown "the period from 6 to 24 months is a period of striking brain changes in the development of autism."

Ninety two infants with autistic older siblings, and so judged to be at risk of developing autism, underwent diffusion-tensor



Mean fiber bundles, with color mapped fractional anisotropy values, for the total sample of 92 infants at risk for autism. Hot colors (red and yellow) represent higher fractional anisotropy values, with blues and purples representing lower values. Figure provided courtesy of Jason Wolff (University of North Carolina, NC, USA).

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imaging, a form of MRI. All infants were scanned at 6-months-old, with many also scanned at 12 and 24 months.

The infants were then assessed at 24 months for behavioral symptoms of autism; 30% of the infants in the study were diagnosed with autism spectrum disorders (ASDs) at this stage.

The MRI data was characterized by fractional anisotrophy, a measure of the development of white matter fiber tracts that shows how organized the fibers are. Fifteen tracts throughout the brain were studied, and of these, 12 were shown to vary in infants that went on to develop ASDs.

However, the differences between infants that develop ASDs and those that do not are not constant throughout development. According to Piven, "we see differences at 6 months of age that are not the same as those seen at 12 months of age, which differ from those seen at 24 months of age." This suggests that future studies will need to take a "developmental approach" to studying brain changes during the early stages of brain development in autistic individuals says Piven.

The large number of tracts found to differ between children that develop ASDs and those that do not has interesting implications for autism research. As Piven explains, "Our findings demonstrate widespread changes in the brain more consistent with theories of changes on a microstructural level (e.g., synaptic density) than identifying a specific location in the brain underlying autism."

He also commented that the findings "demonstrate feasibility of early brain markers being useful in detection of autism prior to the onset of symptoms." Continuing, Piven says that he thinks the results "support the idea of early intervention to prevent or ameliorate the development of symptoms."

However, the authors all agree that more research is needed before this could be used in the clinic, states Piven. "Our findings are still very much in the realm of research findings and do not have any direct implications for clinical practice."

The group are continuing their research and hope to test more subjects, as well as "analyzing many other aspects of our current study with respect to the brain and behavior." Piven also stated that the researchers are hoping to "follow-up the current subjects at a fourth and later time point to clarify diagnosis" and "examine a cohort of younger (than 6 months) children at high risk for autism" in order to further their research.

– Written by Alisa Crisp

Source: Wolff JJ, Gu H, Gerig G *et al.* Differences in white matter fiber tract development present from 6 to 24 months in infants with autism. *Am. J. Psychiatry* doi:10.1176/appi.ajp.2011.11091447 (2012) (Epub ahead of print).

Revised diagnostic criteria for psychiatric disorders may not be welcomed by clinicians

The Diagnostic and Statistical Manual for Mental Disorders is due to be revised, but many physicians do not seem content with what the changes might mean.

The Diagnostic and Statistical Manual for Mental Disorders (DSM), the main source of guidelines for the diagnosis and management of mental disorder, was last revised in 1994, producing the DSM-IV, the form used for diagnosis today.

However, there is much controversy about the use of the DSM to diagnose mental disorders, particularly considering these illnesses are often harder to diagnose than many other types of disease.

DSM does provide some benefit to the international community, as Pinhas Dannon, from Tel Aviv University, Israel, told *Neuropsychiatry*. "We need to talk the same medical language all over the word and DSM provides the language for psychiatrists." However, he suggests that more input from the international community is needed in the revisions, as currently "the system is mainly American Psychological Association classification with less effect from international societies" and "the diagnosis criteria are effected from mainly US experience."

However, it seems that the problems may not be due to the guidelines, but might be more related to our perceptions of mental disorders. According to Randolph Nesse (University of Michigan, MI, USA) "the problem is not the DSM itself, it is that the landscape of mental disorders is far less tidy than we would like it to be." Nesse, talking to *Neuropsychiatry*, explained that unlike in the rest of medicine, we do not adequately understand the physiological functions of the brain to enable us to understand disorders affecting it, meaning that "some complaints about the comorbidity and heterogeneity of DSM diagnoses may arise from unrealistic expectations."

Nesse feels that "the big challenge is how to help clinicians and researchers escape from the tendency to essentialize DSM categories as if they are real entities with real boundaries," and adds that "the tendency to name things and then believe that they really exist as independent entities seems very deep in human cognition."

His suggestion of how to improve the DSM is through "encouraging more realistic expectations." He suggests that "many mental disorders are useful constructs, even if they frustrate the craving for reified categories with sharp boundaries defined by necessary and sufficient conditions."

– Written by Alisa Crisp

Source: Nesse RM, Stein DJ. Towards a genuinely medical model for psychiatric nosology. *BMC Med.* 10(1), 5 (2012).

New evidence suggests depression leads to bullying, contrary to previous opinion

A new study, published in the *Journal of Child Development*, potentially provides evidence against the prevailing view that bullying causes depression in adolescents.

Contrary to the common perception that individuals who are bullied are more likely to develop depression, the study, from Arizona State University (AZ, USA) and the University of Illinois (IL, USA), suggests that adolescents with depressive symptoms are more likely to be bullied later in their school career.

Karen Kocher (Arizona State University), lead author of the study, says that "We examined the issue from both directions but found no evidence to suggest that peer relationships forecasted depression among this school-based sample of adolescents."

The researchers collected information about depressive symptoms, peer relations and victimization through yearly surveys for almost two decades, starting in 1992. Parents, teachers, peers and the students themselves all provided information about some of the various subjects.

Four hundred and eighty six students were included in the study – between fourth and sixth grade. Depression in these students was judged by the presence of depressive symptoms, such as crying or lethargy. Victimization included many different forms of bullying; physical, mental and relational abuse.

The researchers suggest that bullying is due to difficulty with peer relationships, which seems to occur more often in depressed adolescents. Good peer relations at school are important to build a firm base for life's challenges and this research suggests that depression may play an important role. As Kochel says, "If adolescent depression forecasts peer relationship problems, then recognizing depression is very important at this particular age. This is especially true given that social adjustment in adolescence appears to have implications for functioning throughout an individual's lifetime."

To help adolescents through this difficult time, Kochel says that "teachers, administrators and parents need to be aware of the signs and symptoms of depression and the possibility that depression is a risk factor for problematic peer relations."

– Written by Alisa Crisp

Source: Kochel KP, Ladd GW, Rudolph KD. Longitudinal associations among youth depressive symptoms, peer victimization, and low peer acceptance: an interpersonal process perspective. *Child Dev.* doi:10.1111/j.1467–8624.2011.01722.x (2012) (Epub ahead of print).

Computerized cognitive training may help reduce some symptoms of schizophrenia

A new training method may help schizophrenic patients better differentiate between reality and internal experiences.

Karuna Subramaniam and colleagues from the University of California (CA, USA) have demonstrated that using computerized cognitive training improved reality monitoring and possibly social functioning in schizophrenic patients.

The results, published recently in *Neuron,* may have important implications for the treatment of schizophrenia; as Subramaniam explained to *Neuropsychiatry*, the study suggests that "the neural impairments in schizophrenia are not immutably fixed – even in chronically ill individuals who have been ill for more than 20 years – but instead may be amenable to well-designed interventions that target restoration of neural system functioning."

Three patient groups were compared in the study – both schizophrenic patients and healthy controls underwent 80 h of the cognitive training over a period of 16 weeks; schizophrenic controls completed 80 h of computer games in the same time-frame, controlling for computer exposure and social contact during the experiments. Patients were followed-up 6 months after training to judge any continuing impact of the training.

Functional MRI of patients before and after the training also showed that this therapy has a physical effect on the brain, increasing activity in the medial prefrontal cortex "a critical higher-order brain region that supports successful reality-monitoring processes," says Subramaniam. She continues that this is important because "We found that the level of medial prefrontal cortex activation was also linked with better social functioning 6 months after training."

Subramaniam told *Neuropsychiatry* "to our knowledge, it is a first-in-kind demonstration which reveals that by using a 'neural systems-based approach' to cognitive training, it is possible to significantly improve behavioral and brain function in schizophrenia even on an untrained task, such that patients begin to demonstrate more "normal" brain–behavior associations, which in turn predict better social functioning several months later."

Senior author, Sophia Vinogradov commented, "these findings raise the

exciting likelihood that the neural impairments in schizophrenia – and undoubtedly other neuropsychiatric illnesses – are not immutably fixed, but instead may be amenable to well-designed interventions that target restoration of neural system functioning."

– Written by Alisa Crisp

Source: Subramaniam K, Luks TL, Fisher M, Simpson GV, Nagarajan S, Vinogradov S. Computerized cognitive training restores neural activity within the reality monitoring network in schizophrenia. *Neuron* 73(4), 842–853 (2012).

The link between traumatic brain injury and post-traumatic stress disorder is examined in an early-stage proof-of-concept study

A study from the University of California (CA, USA) has examined the link between traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) by studying fear conditioning in rats, a relationship which could be of interest for future clinical research.

The results suggest that it is not just the emotional context surrounding the injury that can lead to an increase in fear in patients, but that there may be a physical link between brain injury and the development of PTSD.

The researchers attempted to dissociate the physical and emotional components of trauma by separating the timing of administration of concussive brain trauma and fear conditioning; rats were conditioned at least 2 days after any injury was administered.

According to Michael Fanselow from the University of California, senior author of the study; "We found that the rats with TBI acquired more fear than control rats (without TBI)." He and other researchers found that "something about the brain injury rendered them more susceptible to acquiring an inappropriately strong fear. It was as if the injury primed the brain for learning to be afraid."

Interestingly the researchers also found a physical manifestation of the trauma in the amygdala. Maxine Reger, first author on the study said "we found that there are significantly more receptors for excitatory neurotransmitters that promote learning" in rats with TBI, suggesting a possible mechanism for the increase in learning fear after TBI – a potential reason for the comorbidity of TBI and PTSD.

Fanselow explained the reasoning behind the study to *Neuropsychiatry*. "Both TBI and PTSD are very prevalent and they also tend to occur together, people with such an injury tend to develop PTSD." One view of why this occurs is that "such physically injurious events are also terribly frightening". However, as Fanselow explains, their study suggests that "it is more than that – the injury predisposes the brain to learn an even stronger fear than it should and we are beginning to understand the physical causes of this relationship."

There are potential implications of this research in clinical practice. Fanselow told *Neuropsychiatry* that "following even a mild brain injury, concussion, say a teenager hurt in a high school football game, we need to be careful and have that person avoid potentially stressful experiences."

The researchers are now looking to learn more about the changes that occur in the brain after traumatic injury, with Fanselow hoping that this will lead us to "develop strategies that can return the brain to normal functioning". In addition, the team hopes to study more permanent changes in the brain by increasing the duration of their experiments.

– Written by Alisa Crisp

Source: Reger ML, Poulos AM, Buen F, Giza CC, Hovda DA, Fanselow MS. Concussive brain injury enhances fear learning and excitatory processes in the amygdala. *Biol. Psychiatry* 71(4) 335–343 (2012).