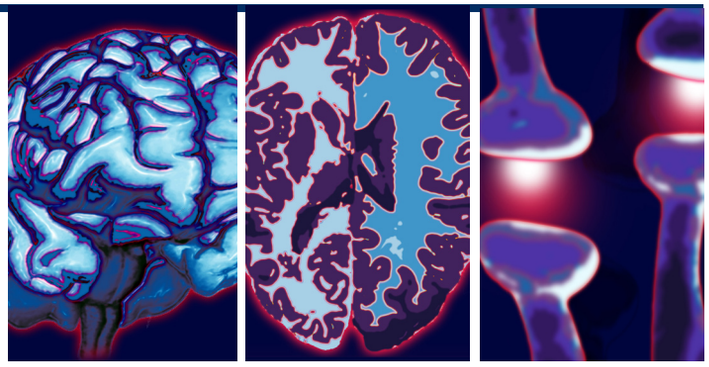

"...depressed mothers showed a reduced positive response to the sound of infant cry compared with controls."

Brain imaging study may indicate a dampened response to an infant's cry in depressed mothers

New findings, published in the journal of *Social Cognitive and Affective Neuroscience*, have begun to uncover some of the differences in brain activity between depressed mothers and nondepressed mothers. The study in question utilized functional MRI to view differences in brain activity in 22 women (11 with depressive symptoms and 11 with no recorded history of depression) in response to a sound played to them in the scanner. The mothers were played one of three sounds, the cry of their own child, a cry of an unknown child or a control sound.

The results demonstrated that depressed mothers showed a reduced positive response to the sound of infant cry compared with controls. This is in contrast to an existing hypothesis, which suggested that depressed mothers may respond in a negative manner to their infant's cries.

"This particular study is important because it is the first to investigate (and find) depression-related differences in mother's brain response to their infants," said Heidemarie K Laurent, first author of the paper and an Assistant Professor at the University of Wyoming (WY, USA).

Nondepressed mothers showed activation in the limbic regions of the brain including the midbrain, striatum and thalamus, key regions of the brain associated with responses to reward and reinforcement. Although depressed mothers also showed activation in these regions, these responses were significantly lower than the nondepressed mothers. In particular, the caudate, nucleus accumbens and medial thalamus showed a much greater activation profile in nondepressed mothers than depressed mothers. As these areas are classically related to reward pathways, Laurent has suggested that this may be a key issue when addressing the response of depressed mothers to their children: "Specifically, it appears that mothers who have a strong history of depression during pregnancy and/or postpartum have trouble associating their baby with reward and are not motivated to approach their baby in the way nondepressed mothers do."

When asked about the impact of the work, Laurent replied: "This work is important because it helps to clarify how and why depressed mothers are responding and parenting differently, informing potential treatment approaches". Although the study was not specifically aimed at finding treatments, these findings may still have an effect upon the treatment

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of depression in mothers. "Clinicians may want to treat depressed mothers similarly to patients overcoming a drug addiction," said Laurent. The study has further implications as it may even help subclinically depressed mothers, "Even mothers who are not suffering from major depression may benefit from interventions to help build their self-regulatory strategies when dealing with their babies," suggested Laurent. "I hope that this research will give both clinicians and family members a better understanding of why and how it is hard for new mothers suffering from depression to be good parents."

Depression in mothers can have a marked impact upon the lives of their children and upon their own wellbeing. When one considers how important a role the mother plays in the caring of a child, it is unsurprising that depression can have detrimental effects upon the psychological and social development of a child.

The study has not only helped the understanding of altered brain processes in depressed mothers, but has also opened the door to new treatment strategies and interventions targeted specifically at depressed mothers.

Source: Laurent HK, Ablow JC: A cry in the dark: depressed mothers show reduced neural activation to their own infant's cry. *Soc. Cogn. Affect. Neurosci.* (2011) (Epub ahead of print).

About the News

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Abnormal motor control of the hands may be a marker for attention-deficit hyperactivity disorder in children

Researchers from the Transcranial Magnetic Stimulation Laboratory at the Cincinnati Children's Hospital (OH, USA) and the Laboratory of Neurocognitive and Imaging Research (Johns Hopkins University, MD, USA) have found a potential new marker for attention-deficit hyperactivity disorder (ADHD) in children.

Two studies published in *Neurology* have examined the responses of children with ADHD and a control population group in a finger tapping task in which the children (25 with ADHD and 25 normal control subjects) were required to sequentially tap their fingers in a left- and right-handed trial. The researchers assessed any 'overflow' movements (unintentional movement of fingers in the opposite hand) through the use of video recording equipment, finding that children with ADHD had over twice as many overflow movements than their corresponding normal counterparts. However, gender analysis demonstrated that this was only significant in boys, and that girls with ADHD did not show a greater tendency for 'overflow' when compared with their normal counterparts. Although this is not the first study to show motor disturbances in children with ADHD, it is the first to quantify movement disorders and ADHD.

"A critical obstacle in ADHD is the lack of quantitative measures of brain function that would provide a basis for more accurate diagnosis and effective treatment," said Stewart Mostofsky, the director of the Laboratory for Neurocognitive and Imaging Research, and the senior author for both papers. "Studying motor control weakness gives us a window to understanding the similar challenges that children with ADHD face in controlling more complex behavior, which can lead to improved diagnosis and treatment".

The second investigation, led by Donald Gilbert the director of the Transcranial Magnetic Stimulation Laboratory in the Cincinnati Children's Hospital, utilized transcranial magnetic stimulation in order to invoke hand twitches in children with ADHD. The researchers then measured the degree of muscle and brain activity, creating a quantifiable measure known as the short interval cortical inhibition (SICI). Children with ADHD demonstrated a reduced SICI (caused by a decrease in motor inhibition) compared with their normal counterparts, with a lower SICI being associated with a greater severity of ADHD symptoms.

"We found SICI to be an important biomarker for predicting ADHD symptoms and severity, and it is a highly quantifiable and reproducible measure. This offers a foundation for determining which children are at a higher risk for severe and ongoing symptoms as they grow older," summarized Gilbert.

It is hoped that in conjunction, these studies could provide a new meaningful diagnostic tool for ADHD and may help improve our understanding of the neurological underpinnings of the disease, allowing a more directed approach to the treatment of ADHD.

Sources: Macneil LK, Xavier P, Garvey MA *et al.*: Quantifying excessive mirror overflow in children with attention-deficit/hyperactivity disorder. *Neurology* 76(7), 622–628 (2011); Gilbert DL, Isaacs KM, Augusta M, Macneil LK, Mostofsky SH: Motor cortex inhibition: a marker of ADHD behaviour and motor development in children. *Neurology* 76(7), 615–621 (2011).

Identification of potential genetic determinant of bipolar disorder

A genetic study published in *Biological Psychiatry* has looked into identifying single nucleotide polymorphisms (SNPs) that may be associated with bipolar disease. Through the analysis of genetic expression levels on post-mortem cortical tissue obtained from patients with bipolar disease, the researchers identified *PCLO* as a potential gene that may contribute to the formation of bipolar disorder.

The study initially compared genetic expression levels in the cortical brain tissue of bipolar disorder patients and from control subjects who did not have a history of bipolar disorder (40 individuals with bipolar disease and 43 control subjects). The results generated 45 potential genes that demonstrated an elevated level of expression in bipolar disease patients. These genes were then investigated in greater detail through the use of SNP marker profiling. SNP rs13438494 was identified as a potential marker for bipolar disorder owing to the high level of association with the disease. This SNP was an intron of the *PCLO* gene, thereby putatively implicating the gene as a determinant of bipolar disorder.

The *PCLO* gene encodes the Piccolo protein, which is expressed at the ends of nerve cells. It is believed to have a role in the release of neurotransmitters and chemical messengers from these cells.

Kwang Choi, the first author of the paper from the Stanley Laboratory of Brain Research (MD, USA) commented on the execution of the study: "We have taken an innovative approach in correlating gene expression with genetic variation data from well characterized post mortem brains and then combining with a large scale meta-analysis of genome-wide association studies."

Further implications of the paper include the importance of this type of study in identifying potential genetic components of complex disorders often found in the field of neuropsychiatry. "If replicated, this study could finally forge a link between gene expression and genome-wide association studies in a complex genetic disorder," said Choi.

When asked about the importance of the paper in the field of psychiatry, the editor of *Biological Psychiatry*, John Krystal responded, "This study is an example of how better knowledge of brain biology may help to guide our genetics studies".

Unravelling the role of individual genes in complex genetic disorders remains a challenging investigative procedure. However, it is hoped that through their identification, more effective forms of diagnosis and targeted treatment can be formulated to deal with bipolar disorder and other complex neuropsychiatric disorders.

Source: Choi KH, Higgs BW, Wendland JR, Song J, McMahon FJ, Webster MJ: Gene expression and genetic variation data implicate *PCLO* in bipolar disorder. *Biol. Psychiatry* 69(4), 353–359 (2011).

Treatment of bipolar disorder with lithium may lead to structural changes in the brain

A new mega-analysis, published in *Biological Psychiatry*, has provided new imaging data on the structural changes in the disease, revealing the differences in the brains of bipolar patients who were either on or off treatment. The research was carried out in a collaborative fashion between eleven research groups. Together, they were able to combine their structural MRI data, to analyze at a high statistical power, the structural differences between the brains of adult bipolar disorder patients and a healthy control population.

Although numerous pharmacological agents exist for the treatment of adult bipolar disorder, lithium remains one of the most efficacious and commonly used interventions in psychiatry for treating the disease. Introduced in the late 1940s it proved to be incredibly effective in the treatment of both the manic and depressive symptoms found in bipolar disorder.

"Although numerous pharmacological agents exist for the treatment of adult bipolar disorder, lithium remains one of the most efficacious and commonly used."

As lithium started to be prescribed more commonly for bipolar disorder, the molecular mechanism by which the drug acted was investigated in animal studies in order to ascertain through what action lithium aided these patients. In conjunction with these studies, imaging

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investigations hinted at alterations in the volumes of certain regions of the brain in bipolar patients.

The team demonstrated that patients who were classed as having bipolar disorder had increased regional brain volumes. These areas included the right putamen, the left temporal lobe and the right lateral ventricular lobe. Bipolar disorder patients also demonstrated a brain volume reduction in the hippocampus and the cerebrum. Furthermore, this cerebral volume reduction was associated with the illness duration of the patients. However, the most important findings were that of the bipolar patient group undergoing lithium therapy. The data collated showed an increase in the hippocampus and the amygdala volumes in these patients taking lithium, greater even than the control group.

This finding not only addresses the typical features seen in bipolar disorder, but also some of the associated features of the disease. Bipolar disorder patients can also have problems with attention and executive functions, which may be connected to the reduction of the cerebrum in these patients. Furthermore, the issues of impaired memory in the disease may be associated with the alterations in hippocampus volume. The use of medication and the alteration to brain volume could explain how these pharmacological agents alleviate some of the problems associated with bipolar disorder.

John Krystal, editor of *Biological Psychiatry*, commented on this study saying: "This important mega-analysis provides strong support for the regional brain structural alterations associated with bipolar disorder, but also sends a signal of hope that treatments for this disorder may reduce some of these deficits".

Source: Hallahan B, Newell J, Soares JC *et al.*: Structural magnetic resonance imaging in bipolar disorder: an international collaborative mega-analysis of individual adult patient data. *Biol. Psychiatry* 64(9), 326–335 (2011).

Study results suggest that addiction-prone women show an increase in depression over time

A longitudinal study published in *Development and Psychopathology*, undertaken by researchers from the Addiction Research Center and Substance Abuse Section (University of Michigan, MI, USA), has looked into the progression of depression in women with a known history of addiction, finding that this vulnerable proportion of society is more likely to have a worsening of their depression despite a reduction in other social problems.

The study, which followed a sample of 273 adult women (aged between 30 and 40) over 12 years, investigated numerous aspects of their social lives in order to ascertain what risk factors affected their levels of depression, alcoholism and antisocial behavior.

The results showed a clear increase in depression in these women over time, in contrast to their levels of alcoholism and antisocial behavior, which showed a definitive decrease over time. The study suggested that the severity and increase in depression may be associated with the instability of the local area (e.g., how frequently neighbors relocate in the surrounding region). Furthermore, the behavior of the mothers' children had a significant impact on levels of depression. Increased levels of isolated and sad emotions in the children resulted in increases in depression in their respective mothers.

Rather than adhering to existing theories that depression or antisocial behavior is attributable to genetics or the environment, Robert Zucker, the head author of the paper and the director of the Addiction Research Center and Substance Abuse Section, suggests an alternative hypothesis: "It's really the network of these relationships, at the biological, social and at the community level – that influences these disorders over time."

There seems to be a fundamental difference in the progression of depression when compared with the corresponding changes in alcoholism and antisocial behavior. "Unlike the other two disorders, biological differences appear to be more of a constant factor in depression," said Zucker. Understanding the key factors that affect depression in this population of particularly vulnerable women can allow tailored interventions to reduce their levels of depression. "Based on these findings, interventions for women with young children might have the most impact if they improve social supports, educational opportunities, access to family counseling and neighborhoods environments," said Anne Buu, lead author of the paper.

It is clear that these longitudinal studies are useful in determining possible areas of interventions, particularly in high-risk groups. It is hoped that through the identification of the most crucial social determinants of depression, effective treatments can be formed to aid these patients.

Source: Buu A, Wang W, Wang J, Puttler LI, Fitzgerald HE, Zucker RA: Changes in women's alcoholic, antisocial, and depressive symptomatology over 12 years: a multilevel network of individual, familial, and neighborhood influences. *Dev. Psychopathol.* 23(1), 325–327 (2011).