Depression issue

Determining the “IMPACT” of therapeutics for depression requires an adaptive trial design - Practitioner Review
Professor Ian Goodyer, Dr. Paul Wilkinson

Are there sub-groups of children characterized by similarities in the development of depressive symptoms?

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Accelerated cortical thinning correlates with early signs of depression

By Dr Jessica K Edwards

The brain undergoes structural changes as it develops over childhood, but whether abnormal structural changes are associated with emerging depressive symptoms in adolescence is unknown. Now, a longitudinal study that enrolled 205 participants aged 8-25 years without signs of depression has used magnetic resonance imaging (MRI) to monitor these brain changes over adolescence. The participants underwent MRI every 2 years over a 5-year period to monitor changes in cortical thickness, surface area and sub-cortical volume. At the third MRI, depressive symptoms were assessed by self-report (Beck Depression Inventory II). Those who had developed depressive symptoms by this time point, showed accelerated frontal lobe cortical thinning compared to those without depressive symptoms. Interestingly, changes in hippocampal and amygdala volume were not associated with depressive symptoms, despite previous studies suggesting a potential link between volumetric differences in these brain regions and depression. The researchers also noted that accelerated cortical thinning in adolescence has previously been associated with positive behavioural outcomes, such as improved cognitive performance, yet here it was associated with an adverse outcome. The researchers propose that accelerated frontal lobe cortical thinning may be associated with emerging depressive symptoms in adolescence.


Further reading:

Glossary:
- Magnetic resonance imaging: a non-invasive technique that uses a strong, static magnetic field and radio waves to measure brain activity

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Depression is highly prevalent but under-reported in children with ADHD

By Dr Jessica K Edwards

Researchers at Cardiff University have investigated whether the symptoms of depression observed in patients with attention-deficit/hyperactivity disorder (ADHD) differ from those reported in the general population. The study recruited 249 children with ADHD (mean age 14.6 years) and a large general population sample of 2460 individuals (mean age 12.8 years) to compare (i) the prevalence of depression symptoms, (ii) the depression symptoms most commonly reported and (iii) the child-reports and parent-reports of depression symptoms. Parents and children completed the Mood and Feelings Questionnaire (MFQ), which consists of descriptive phrases regarding how a subject has been feeling recently, and must be scored as either "true", "sometimes true" or "not true". The total parent-reported MFQ and child-reported MFQ scores were then calculated and compared. The average parent-reported and child-reported MFQ scores were significantly higher in the ADHD sample compared to the general population, indicating that depression symptoms were more common in those with ADHD. The overall profile of depression symptoms in ADHD, however, was similar to the general population with feelings of irritability, restlessness, difficulties with concentration and being unhappy reported most often by both groups. Interestingly, parents of children with ADHD were more likely to report symptoms of depression than their child, whereas the reverse was true in the general population. This finding suggests that children with ADHD tend to under-report depression symptoms compared to the general population. The researchers conclude that depression symptoms are highly prevalent in ADHD, and exhibit a similar profile to the depression symptoms observed in the general population.


Further reading:

Glossary:
- Mood and Feelings Questionnaire (MFQ): A questionnaire containing 33 questions to capture the symptoms included in the DSM-IV criteria for major depressive disorders. It is considered an appropriate assessment tool for depression symptoms in children aged range 8–18 years, but not a method to diagnose depression. The questions assess mood and emotional, ideational, restlessness, concentration difficulties, and several aspects of negative self-evaluation. A high MFQ suggests more severe depressive symptoms.
The overlap between low self-esteem and anxiety/depression in CAMHS

By Loades, M.E.1,2

Young people presenting to CAMHS often report problems with ‘low self-esteem’. Self-esteem can be thought of as the overall opinion or evaluation we have of ourselves, including the judgements we make about ourselves and the value we attach to ourselves. Questionnaires like the Rosenberg Self-Esteem Scale can be used to assess self-esteem. There is a complex relationship between self-esteem and mental health problems. It is possible that low self-esteem can be a vulnerability factor, predisposing a person to developing a mental health problem. It is also possible that low self-esteem can result from mental health difficulties and their sequelae (e.g. the negative thinking about the self in depression). This complexity is further complicated by the conceptual overlap between the main constructs of low self-esteem and depression, and their associated measures.

Cognitive Behavior Therapy (CBT) for low self-esteem has shown promise as a broadly applicable intervention in adults, tackling difficulties with anxiety and low mood at the same time. It is based on the CBT model of low self-esteem, developed by Melanie Fennell and colleagues. Treatment is driven by an individualised formulation, and involves identifying and challenging negative beliefs about the self, referred to as the ‘bottom line’ (e.g. ‘I am worthless/unlovable’), and also noticing and logging positive evidence about the self and one’s positive qualities and strengths. So far, this approach has not been tested in young people. To make the case to test it, clarity is needed about the extent to which low self-esteem is associated with ‘clinically significant’ anxiety and depressive disorders in young people (that is, anxiety or depression which meets full diagnostic criteria). Furthermore, it is also important to know the extent to which low self-esteem in young people poses a vulnerability for subsequent mental health difficulties, which would strengthen the argument for treating it as a preventative measure.

Our systematic review aimed to establish what is known about low self-esteem and anxiety/depression in young people (children). We wanted to find out whether young people with clinically significant anxiety disorders and/or depression also have low self-esteem as measured on validated questionnaires. We also wanted to know whether young people with low self-esteem as measured on a validated questionnaire develop depression and anxiety symptomology later in adolescence and young adulthood. To address these questions, we systematically searched electronic databases to identify relevant studies. We found 10 studies which looked at the co-occurrence of low self-esteem and clinically significant anxiety/depression. These studies included young people recruited from the community and inpatient and outpatient mental health services. Young people with depression tended to report lower self-esteem than those with anxiety disorders, while those with both anxiety and depression were found to have the lowest self-esteem. Young people with any mental health problems tended to have lower self-esteem than those who do not have mental health problems.

We found 8 studies which reported on the association between low self-esteem in young people and anxiety/depression symptoms in the subsequent 1 to 6 years. From these studies, low self-esteem in young people appeared to be a relatively weak predictor of the development of anxiety and depression in later adolescence and early adulthood. Several studies reported a significant association, although with a relatively small effect, between low self-esteem and subsequent depressive symptoms. For example, Trzesniewski and colleagues (2006) reported that adolescents with low self-esteem were 1.26 times more likely to develop Major Depressive Disorder by the age of 16 than healthy adolescents. This pattern remained even when other vulnerability factors for developing depression (e.g. baseline depression, socio-economic status and IQ) were taken into account. However, other studies did not find the same association, most likely because the link between self-esteem and later depression is complex and multi-faceted, and likely to be influenced by the accumulation of multiple risk factors. Fewer studies reported on later anxiety. Interestingly, Trzesniewski et al. (2006) found that adolescents with low self-esteem were 1.6 times more likely to develop an anxiety disorder.

The studies we reviewed suggest that young people with clinically significant anxiety or depression, and particularly those with co-morbid anxiety and depression are also likely to have low self-esteem. Further research into the utility of the CBT model of low self-esteem and treatment based on this transdiagnostic model in young people is indicated. A number of smaller scale case series may be helpful to first establish whether a larger trial of CBT is indicated.

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Determining the “IMPACT” of therapeutics for depression requires an adaptive trial design

By Dr. Jessica K. Edwards

A large proportion of adolescents suffering from moderate-to-severe major depression respond to psychological and pharmacological therapy, and the range of effective treatment modalities is increasing. Now, Ian Goodyer and Paul Wilkinson have compiled a Practitioner Review that compares the various treatment options available and assesses their effectiveness for adolescents affected by major depressive episodes.

In 2010, Professor Ian Goodyer and Dr. Paul Wilkinson together with their colleagues around the UK launched the Improving Mood with Psychoanalytic and Cognitive Therapies (IMPACT) study to determine the cost-effectiveness, safety and relapse rates of three treatment regimens known to reduce depressive symptoms. Specifically, they compared cognitive behavioural therapy (CBT) and short-term psychoanalytic psychotherapy (STPP) delivered over 5-7 months by specialists trained in these modalities, with a novel reference treatment of brief psychosocial intervention (BPI) delivered at low intensity within 3 months by psychiatrists and mental-health nurses. In 2017, the first published results from the IMPACT study indicated that neither CBT nor STPP were superior to each other, and that BPI was equivalent to both in maintaining reduced self-reported depression symptoms 1 year after treatment completion.

In their 2018 Practitioner Review for the Journal of Child Psychology and Psychiatry, Goodyer and Wilkinson assessed the current state of knowledge on treatment modalities for major depressive episodes in adolescents and how the published data compared with the key findings of the IMPACT study — that BPI may be as good as accepted specialist CBT therapy or STPP. Their findings predominantly derive from four key randomized controlled trials (RCTs) that report on psychological and pharmacological treatments for depressed adolescents, and a set of studies that looked at prevention of the onset of major depressive disorder.

First focusing on psychological therapies, Goodyer and Wilkinson found that although promising results from RCTs have favoured CBT and interpersonal psychotherapy (IPT), a recent meta-analysis found their effect size to be relatively small (0.29) compared to active control groups. The reasons behind this low effect size may be because of improvements in methodology and better active control treatments since the first RCTs of CBT and IPT were established. By contrast, another meta-analysis did find CBT and IPT to be efficacious and clinically effective in adolescents with depression. The researchers of both these meta-analyses noted that the number of IPT studies and sample sizes are too low to draw firm conclusions.

The IMPACT study, however, was sufficiently powered to examine whether specialist therapies exert therapeutic gains over those expected from a relatively simple active approach (BPI) delivered via a manual. “The results of IMPACT were thus surprising and in stark contrast to previous opinion in showing that all three psychological treatments (CBT, STPP and BPI) had potentially equal clinical effectiveness at the end of treatment and at 12-months follow-up,” explains Goodyer. Early evidence indeed suggested that BPI may be effective for mild-to-moderate depression and anxiety disorders in adolescents. Now, further work must assess the effectiveness of the BPI method used in the IMPACT study in a community, rather than a clinical setting.

In 2010, Goodyer and Wilkinson then turned their attention to the therapeutic effects elicited by antidepressants. Here, they found that the most robustly designed studies showed that antidepressants can achieve an efficacy up to 20-35% higher than placebo. Some selective serotonin reuptake inhibitors (SSRIs), most notably fluoxetine, elicit strong effects over placebo, but other antidepressants (e.g. mirtazapine and venlafaxine) have no proven effects. Furthermore, data suggest that SSRIs may increase suicidal thinking in some adolescents with depression: in rare cases, fluoxetine can induce disinhibition and switching to mania. More trials that recruit patients with severe depression are needed to deeply evaluate SSRI efficacy and determine any potential adverse effects.

Goodyer and Wilkinson next assessed treatment response, treatment non-response and relapse for the aforementioned therapeutic approaches. Response rates in treatment-naive adolescents with depression are usually fairly rapid, with up to 30% reduction in symptoms achievable in the first 12 weeks of starting some form of treatment. Remission rates are also high, with reportedly 80% of trial patients remaining in clinical remission (no diagnosis or persistent 50% reduction in baseline symptoms) for up to 1 year after treatment end.

“up to 30% reduction in symptoms achievable in the first 12 weeks of starting some form of treatment”

Unfortunately, relapse rates are high (50-75%) in successfully treated patients. As such, Goodyer and Wilkinson recommend that clinical monitoring should be continued for an additional 6 months after treatment, or until at least a 50% drop in symptoms is reached. They also suggest that “booster” psychological treatment sessions could be offered to those showing early signs of relapse.

In those who do not show any initial response to treatment (up to 40% adolescents), a combination treatment strategy should be recommended that employs both psychological and pharmacological treatment modalities. “Treatment is effective, be it psychological or pharmacological, for about two thirds of patients”, reinforces Goodyer. “Clinicians should make good assessments and choose collaboratively with the patient what treatment to use. There is no reason to not treat all patients”.

Although no demographic factors have been identified that can reliably predict these described differences in treatment outcome, clinical severity at baseline may be associated with a poor treatment response. Parameters at first assessment associated with clinical severity of depression include poor global functioning, high levels of suicidality, co-morbid anxiety, cognitive distortions, hopelessness and family conflict.
It is a complex design, but will help answer that key works for which subtype of depression,” says Goodyer. Established that will disaggregate what treatment the needs of the individual patient. “Going forward for adolescents with depression that is tailored to a precision medicine approach needs to be adopted also urgently needed. Ultimately, they consider that what treatment works for whom. Studies that aim is still lacking as to how any treatment works and placebos alone. The authors explain that knowledge identified to reduce the incident onset of depression in there are currently no clear strategies that have been large sample size and a long study duration, as well as lack of power and high costs. In summary, Goodyer and Wilkinson note that while acknowledging prevention is better than a cure, there are currently no clear strategies that have been identified to reduce the incident onset of depression in this population. However the data so far does indicate that major depressive episodes are highly treatable, with active therapies being more effective than active placebos alone. The authors explain that knowledge is still lacking as to how any treatment works and what treatment works for whom. Studies that aim to identify new medications and/or psychological therapies for severely treatment-resistant cases are also urgently needed. Ultimately, they consider that a precision medicine approach needs to be adopted for adolescents with depression that is tailored to the needs of the individual patient. “Going forward scientifically, we recommend that adaptive trials be established that will disaggregate what treatment works for which subtype of depression,” says Goodyer. “It is a complex design, but will help answer that key question better than any trial has done to date.”

The trajectories of depressive symptoms expressed in early childhood differ between boys and girls

By Dr Jessica K Edwards

A study by Diana Whalen and colleagues at Washington University has used latent class analysis (LCA) to identify and define the trajectories of latent classes of depressive symptoms in early childhood. The study included 548 children from the Preschool Depression Study, who across a 10-year period completed at least three behavioural assessments. The researchers assessed symptoms of depression and oppositional defiant disorder/conduct disorder (ODD/CD) diagnoses using the Preschool Psychiatric Assessment (PPA), as well as social risk factors, family history of affective disorders and functional impairment. The researchers identified three trajectories of depressive symptoms based on high, medium and low symptom severity in boys and girls. Interestingly, the high depression severity latent class in boys was characterized by an increase in symptom severity from preschool through to school age, and then a decline during later school age. For girls, however, the high depression severity latent class was characterized by stable symptom severity over time. Early childhood social adversity, family history of affective disorder, preschool onset of ODD/CD and school age functional impairment differentiated the high-risk trajectory classes among boys and girls. Finally, the researchers reported that early childhood social adversity prior to age 5 could predict greater depressive symptom severity across preschool and into school age in girls and boys.
Longitudinal trajectories of child and adolescent depressive symptoms and their predictors - A systematic review and meta-analysis

By Lori Shore B.A, Grad Dip. Couns. Psych., M. Comm, M. Psych (Clin), PhD Clinical, Counselling and Organisational Psychologist


Are there sub-groups of children characterized by similarities in the development of depressive symptoms? And, if there are, could this be a basis for early intervention and prevention of depressive disorders? Through a systematic review the researchers (Shore et al., 2017) identified five subgroups of children and adolescents that can be reliably identified in longitudinal studies based on commonalities in their depressive symptom development. After adjusting the studies to characterize child depressive symptoms into a similar metric, the researchers identified: 56% of children followed a ‘No or child depressive symptoms into a similar metric, the development. After adjusting the studies to characterize based on commonalities in their depressive symptom scores were recalibrated across studies to unique statistical methodology that groups individuals based on common symptom patterns over time. Individual and group differences are then explained by theory, sociodemographics, genotype, other biomarkers, and psychosocial predictors. Twenty English language longitudinal studies in nonclinical populations conducted between 2002 and 2015 were included. The combined study population was 41,256 with a baseline age of <19 years. The potential influence of puberty on the development of depression in the studies was examined. The studies were divided into those with a baseline assessment either prior to secondary school (ages 6–11 years) or post primary school (ages 11–16 years).

The initial analysis revealed between three and 11 depressive symptom trajectories in the published studies we included. However, these were not comparable because of the inconsistency in measures of depressive systems. At least 10 measures of depressive symptoms, with varying cutoff scores, were evident across studies. Therefore, depressive symptom scores were recalibrated across studies to equate to the most commonly used measure – the Centre for Epidemiological Studies Depression scale (CES-D). A random-effects meta-analysis then identified five common depressive symptom trajectories across the studies. Across the studies moderate symptoms were associated with poorer adjustment and outcomes relative to low symptom groups, even though the studies varied in sample, methods, and measures. This suggested that differences in child and adolescent depressive symptom patterns over time are robust. This has implications for the diagnosis of depression in children and adolescents, particularly in relation to the classification of adult clinical mental health disorders.

Through a systematic review the researchers identified studies that adopted trajectory modeling to examine depressive symptoms in children and adolescents, and the predictors. Unlike other types of longitudinal or cross-sectional analysis, trajectory modeling is a unique statistical methodology that groups individuals based on common symptom patterns over time. Individual and group differences are then explained by theory, sociodemographics, genotype, other biomarkers, and psychosocial predictors. Twenty English language longitudinal studies in nonclinical populations conducted between 2002 and 2015 were included. The combined study population was 41,256 with a baseline age of <19 years. The potential influence of puberty on the development of depression in the studies was examined. The studies were divided into those with a baseline assessment either prior to secondary school (ages 6–11 years) or post primary school (ages 11–16 years).

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In summary, differing developmental trajectories of depressive symptoms may be underpinned by several distinct psychosocial and neurodevelopmental factors. This means that the interaction of social, psychological, and biological factors over time sets some children on divergent developmental trajectories. Understanding those predictors and providing early intervention strategies to children may support increased membership of the low or no depressive childhood symptom trajectories. In doing so this will go some way to reduce the risk of chronic depression and other adverse outcomes.

Author statement:
Dr. Lori Shore is a Clinical, Counselling and Organisational Psychologist who has worked extensively in private and public settings as well as within the higher education sector. She holds a PhD, a Master of Clinical Psychology and a Master of Commerce and has published and presented research both locally and internationally. Dr Shore has a close affiliation with the School of Psychology at Deakin University, Victoria Australia.
Offspring of mothers with depression show asymmetric frontal brain activity

Frontal asymmetry (FA) describes differences in engagement between the left and right frontal brain, and is measured in terms of alpha wave-band frequencies. Numerous studies have linked depression with FA, specifically reduced left frontal alpha-band activity³, and suggested that FA may be a vulnerability marker for depression². Thus, researchers have proposed that FA should be evident in the offspring of depressed parents, but the supporting data thus far are unclear. Researchers have now assessed this hypothesis longitudinally, by measuring FA (by electroencephalography, EEG) in a sample of 253 children with no prior diagnosis of depression at ages 3 and 6 years. Maternal history of depressive disorders was determined using the Structured Clinical Interview for DSM-IV Non-patient (SCID-NP) edition at the first EEG, and child depressive disorder diagnoses were evaluated using the Preschool Age Psychiatric Assessment (PAPA). The researchers found a significant interaction between maternal depression and child age, whereby offspring of mothers with depression developed significantly reduced left frontal alpha-band activity compared to right frontal activity over time. By contrast, offspring of mothers without a history of depression showed symmetrical frontal brain activity at both time points. These findings highlight the importance of a longitudinal study design in delineating brain activity at both time points. These findings highlight the importance of a longitudinal study design in delineating brain activity at both time points.

Notes: