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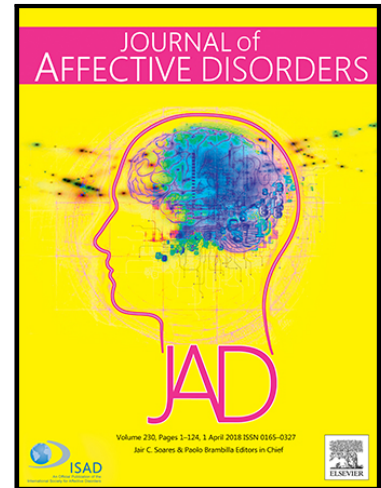
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Accepted Manuscript

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Highlights

- There are etiological and treatment differences between adult and adolescent depression
- We systematically compared adolescent and adult major depression symptom profiles
- Appetite/weight change, energy loss and insomnia were common in adolescents
- Loss of interest/anhedonia and concentration problems were more common in adults
- Results were similar for Major Depressive Disorder and depressive symptom count

ACCEPTED MANUSCRIPT

Adolescent and adult differences in major depression symptom profiles

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ABSTRACT

Background

Depression is the leading global cause of disability and often begins in adolescence. The genetic architecture and treatment response profiles for adults and adolescents differ even though identical criteria are used to diagnose depression across different age groups. There is no clear consensus on how these groups differ in their *symptom* profiles.

Methods

Using data from a two-generation family study, we compared the presentation of DSM-IV depressive symptoms in adolescents and adults with MDD (Major Depressive Disorder). We also compared DSM-IV depressive symptom counts using latent class analysis.

Results

Vegetative symptoms (appetite and weight change, loss of energy and insomnia) were more common in adolescent MDD than adult MDD. Anhedonia/loss of interest and concentration problems were more common in adults with MDD. When using latent class analysis to look at depressive symptoms, a vegetative symptom profile was also seen in adolescent depression only.

Limitations

Adults and adolescents were recruited in different ways. Adolescent cases were more likely to be first-onset while adult cases were recurrences. It was not possible to examine how recurrence affected adolescent depression symptom profiles.

Conclusion

Differences in how depression presents in adolescents and adults may be consistent with different pathophysiological mechanisms. For adolescents, we found that

vegetative/physical disturbances were common (loss of energy, changes in weight, appetite and sleep changes). For adults, anhedonia/loss of interest and concentration difficulties were more common.

Key words: depression, adolescent, child, adult, profile, vegetative

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Introduction

Major depressive disorder (MDD) affects 350 million people worldwide and is the single largest contributor to years lived with disability (Vos et al., 2012). It is the top cause of disability in adolescents and young adults. During adolescence, the incidence of depressive symptoms and MDD increases sharply (Thapar et al., 2012). Adolescence is a risk period for the onset of depression with high recurrence rates and poor functional outcomes (Dunn and Goodyer, 2006).

Identical diagnostic criteria are used to define major depressive disorder in adults and in children/adolescents. The one exception to this is that DSM-IV and 5 (APA, 2000, 2013) allow irritable rather than depressed mood as a core diagnostic mood symptom for children/adolescents. The use of the same diagnostic criteria in adults, children and adolescents implies that the presentation of the disorder is age-independent. Indeed, there is evidence to support the suggestion that, in terms of risk factors, neural correlates and continuity over time, adolescent-onset MDD can be viewed as an early-onset form of the adult disorder (Maughan, Collishaw & Stringaris, 2013; Rutter, Kim-Cohen & Maughan, 2006; Thapar et al., 2012). Nevertheless, there are important aetiological differences between adolescent and adult disorder in terms of treatment response and genetic architecture. The evidence for the effectiveness of antidepressants in treating adolescent depression is sparser than that for adult depression. In particular, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants show smaller effect sizes in treating depression in adolescents compared to adults (Hazell et al., 1995; Hazell & Mirzaie, 2013; Locher et al., 2017; Thapar et al., 2012). This may be partly due to a higher placebo response for depression in young people (Janicud et al., 2017). Third generation antidepressants such as SNRIs and mirtazapine have not shown to be significantly better than placebo (Thapar et al., 2012; Locher et al., 2017). Interestingly, the effect size for Cognitive Behavioural Therapy also appears to be lower for adolescent than adult

depression (Weisz et al., 2017). Studies also suggest that there is genetic heterogeneity of depression according to age of onset such that a relatively earlier age of onset is more strongly associated with alleles that confer risk for bipolar disorder and schizophrenia compared to later onset depression (Power et al., 2017; Verduijn et al., 2017). Similarly, evidence from twin studies suggests genetic differences between paediatric and adult depression (Lau and Eley, 2010; Rice, 2010; Rice et al., 2002). Collectively, evidence suggests aetiological differences between adolescent and adult depression.

Clinical descriptions of major depressive disorder (MDD) in adolescents also suggest possible differences in the presentation compared to that in adults. In particular that specific vegetative symptoms including appetite and weight disturbance, fatigue and insomnia may be particularly common in clinically depressed children and adolescents (Goodyer and Cooper, 1993; Nardi et al., 2013; Roberts et al., 1995; Ryan et al., 1987). Interestingly, hypersomnia appears less common in young people (Kovacs, 1996). Somatic symptoms which refer to unexplained physical complaints such as musculoskeletal pain or headaches have also been reported as being particularly common in clinically depressed children and adolescents (McCauley et al., 1991; Nardi et al., 2013; Ryan et al., 1987). Probably the largest study of symptom profiles in adolescent depression involved using item response theory to assess the relationship of depressive symptoms to the underlying dimension of depression (Cole et al., 2011). That study identified concentration problems, feelings of worthlessness/guilt and sleep disturbance as present at low levels of depression severity, while psychomotor agitation/retardation, weight and appetite change and suicidal ideation or attempts were present only at high levels of depression severity (Cole et al., 2011).

Nonetheless, interpretation of these potential differences in the presentation of MDD between adolescents and adults is obscured due to between-study inconsistencies in how symptoms are assessed and the lack of studies that directly compare adult and adolescent MDD symptoms using similar assessment and recruitment methods. Indeed, it has been highlighted that comparisons have been unsystematic (Kovacs, 1996). There is a need for

studies that directly compare the presentation of depressive symptomatology in adolescents to adults in samples using comparable recruitment and assessment methods. A consideration of depressive symptoms would also be informative given that these are functionally impairing, frequently occur in between 'full-blown' episodes of clinical depression and predict subsequent major depressive episodes both in adolescents and adults (Angold et al., 1999; Johnson et al., 1992; Judd et al., 1998; Pickles et al., 2001).

In a large study of depression where adults with a history of recurrent MDD and their adolescent offspring were rigorously assessed using similar clinical diagnostic interviews on three occasions, we examined the following research questions:

1. Are there differences in the symptomatology exhibited by adults and adolescents with a diagnosis of major depressive disorder?
2. Are there differences in the profiles of depressive symptoms exhibited by adults and adolescents?

Methods

This study utilised data from the 'Early Prediction of Adolescent Depression' (EPAD) study which includes 335 adults with recurrent Major Depressive Disorder (MDD) and their adolescent offspring. All adults had a history of two or more major depressive episodes, were recruited mainly from primary care and had a biological child living at home aged 9-17 years at baseline (Mars et al., 2012). The sampling strategy involved recruiting adults with recurrent MDD who at baseline were living with a child within the study age range (9 to 17 years) to whom they were biologically related. Prior to participation, adults were screened by the research team over the telephone to ensure their family fulfilled the inclusion criteria. These were: recurrent unipolar depression in the parent (at least 2 episodes; later confirmed by diagnostic interview) but the parent need not have been experiencing a depressive episode at the time of recruitment. Living with a biological child in the age range of the study. Parents with a psychotic or bipolar diagnosis and those who met DSM-IV criteria for mania/hypomania at the time of interview were excluded from the study. Families were also excluded if the participating child had moderate–severe intellectual disability (IQ <50). There were no diagnostic exclusion criteria for the children at study entry. Clinical interviews of the parent's and the adolescent's current mental state were undertaken on three occasions at approximately annual intervals.

At each adult assessment, diagnosis of DSM-IV MDD during the preceding month was based on a semi-structured interview, the Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990). All interviewers were trained in the use of the SCAN and diagnoses were discussed at clinical consensus meetings led by a consultant psychiatrist (DJS). Adults reported on family history of depression and other major psychiatric disorders in first and second degree relatives.

In the adolescents, depressive symptoms were assessed with the Child and Adolescent Psychiatric Assessment (CAPA) (Angold and Costello, 2000) which is a semi-structured

diagnostic interview that derives psychiatric symptoms and diagnoses during the preceding 3 months. The parent and child assessments were completed independently by trained, supervised interviewers. Diagnosed and sub-threshold cases were reviewed by two experienced child and adolescent psychiatrists (AT and RP). MDD in adults and adolescents was defined as the presence of at least 5 depressive symptoms, including one of the core symptoms of low mood or irritability or loss of interest/pleasure plus depression-related impairment. Symptoms were derived from the respective interviews for adolescents and adults. In general, symptoms were tapped by similar questions with slight differences in language to ensure the interviews were age appropriate. For instance, in the CAPA, depressed mood was prompted by asking about “feeling unhappy, miserable, blue, low spirited, being down in the dumps or dejected” while in the SCAN depressed mood was prompted by asking about “feeling low in spirits, describing mood as sad, downcast, gloomy, despairing or deeply depressed.” In terms of thresholds and durations for symptoms to be endorsed, these were broadly similar across the CAPA and SCAN. For example, for insomnia to be endorsed a reduction in sleep of over 1 hour was required for both interviews. Slight differences in questions and thresholds were observed for loss of energy (where the CAPA asked about tiredness, fatigability and subjective loss of energy while the SCAN asked about loss of energy and for concentration where the CAPA asked about inefficient thinking and indecisiveness and the SCAN asked about loss of concentration and subjectively inefficient thinking). Otherwise, items were very similar across the interviews for young person and adult.

The primary outcome variable was the cumulative prevalence of MDD defined as the presence of an episode of MDD at any of the three assessment points over the course of the study. Where individuals met criteria for current MDD at more than one of the three assessments, the first episode was selected. 109 (32.5%) adults and 37 (11%) adolescents met DSM-IV diagnostic criteria for current MDD on at least one occasion over the course of the study. The secondary outcome variable was DSM-IV depressive symptom count.

Analyses of depressive symptoms included participants with at least one DSM-IV depressive symptom (233 adults (69.9%) and 236 adolescents (70.4%)) as this was required for latent class analysis.

Statistical analysis

We first examined rates of symptom endorsement in adult and adolescent MDD groups using odds ratios (OR). Odds ratios greater than one denoted that a symptom was more common in the adolescent group. P values were FDR (false discovery rate) corrected for multiple comparisons. Where evidence of differences in symptom frequency between adolescents and adults with MDD were found, sensitivity analyses were conducted to investigate the role of: age (comparing unaffected adolescents vs. unaffected adults), family history (comparing adults with vs. without a parent with MDD), gender (female participants only) and informant (adolescent self rated symptoms only). For analyses that required comparison to unaffected participants, data from the first study time-point were used. Analyses utilising adolescent self-reported depressive symptoms were also run as a sensitivity check to examine any potential effect of informant. Next, we examined the pattern of adult and adolescent depressive symptoms using latent class analysis (LCA) in MPlus (Muthén and Muthén, 2012). Latent class analysis (LCA) is a “person-centred” approach that aims to group similar individuals into “classes” (categories). This thus allowed us to examine the patterns of symptom profiles for adults and adolescents. In line with most recommendations we selected the optimal models on the basis of a number of factors including the meaning and interpretability of classes based on existing knowledge and theory; fit indices and the size of the smallest class – a minimum of around 5% of the sample (Jung & Wickrama, 2008). To select the number of classes for the LCAs, we modelled k-class solutions, modelling subsequent k+1 solutions until the optimum solution was reached. We used the sample size adjusted Bayesian information criterion (ssaBIC) to identify the best fitting models (Berlin et al., 2014). In adolescents, the ssaBIC decreased across the 1-, 2- and 3-class solutions (ssaBIC = 2627.18, 2490.08 and 2480.60 respectively), before

increasing for the 4-class solution (ssaBIC= 2487.94). Consistent with this, the bootstrap likelihood ratio test (BLRT) showed that fit improved when including an additional class until the three class solution with no further improvement in fit when adding a fourth class (BLRT $p = .1579$). Thus the 3-class solutions was selected. In adults, the ssaBIC decreased across the 1-, 2-, 3- and 4-class solutions (ssaBIC = 3425.30, 3016.33, 2997.11 and 2990.83 respectively), before increasing for the 5-class solution (ssaBIC=2993.62). Consistent with this, the BLRT showed that fit improved when including an additional class until the four class solution with no further improvement in fit when adding a fifth class (BLRT $p = 1$). Thus the 4-class solutions was therefore selected. Both the adolescent and adult models had high entropy (0.96 and 0.83 respectively). Associations between the classes and MDD were investigated using the 'best-guess' class (Berlin et al., 2014; Muthén and Muthén, 2012).

Results

Depressive symptoms in adolescent and adult MDD

109 adults (mean age= 41.5 years, range= 26-55) and 37 adolescents (mean age= 14.2 years, range = 10-18) met DSM-IV diagnostic criteria for current MDD at least once during the study. We compared the frequency of 10 DSM-IV depressive symptoms in the adolescents and adults where comparable data were available for both adolescent and adult samples (with appetite/weight change and sleep disturbance additionally disaggregated into increased or decreased appetite/weight and hypersomnia and insomnia) (Table 1). As expected, all depressive symptoms were more common in those individuals with a diagnosis of MDD than those without. The mean total number of symptoms was similar in adults and adolescents with MDD (7.1 vs 7.5) with both groups exhibiting severe MDD (WHO, 1992). The most common *core* DSM symptom exhibited by both adults and adolescents with MDD was depressed mood (Table 1). The core symptom of loss of interest/anhedonia was more commonly observed in adult than adolescent MDD. In terms of the core symptom of irritable mood, no significant difference in the prevalence in adolescents with MDD (17%) and adults with MDD (30%) was observed. In the adolescent MDD group, irritable mood was not present in any individual in the absence of depressed mood.

In adolescents with MDD, the symptoms of loss of energy (97.2%), depressed mood (94.6%), insomnia (reduction in sleep by at least 2 hours per night; 86.5%) and worthlessness/guilt (81.1%) were very common. In adults with MDD, the symptoms of depressed mood (98.2%), loss of interest/anhedonia (88.1%) and worthlessness/guilt (85.2%) predominated. While worthlessness/guilt was commonly endorsed in both adult and adolescents with MDD, several differences in symptom prevalence were observed. Thus, as shown in Table 1, four symptoms were more common in adolescents with MDD: change in appetite, weight gain, weight loss, insomnia, loss of energy. In contrast, two symptoms were more common in adults with MDD: loss of interest/anhedonia and loss of concentration.

Table 2 shows the results of sensitivity analyses to check whether observed differences between adolescent and adult MDD were attributable to age, family history, gender (females only). The pattern of results largely remained the same. The exceptions to this were that (a) loss of interest/anhedonia was in part more common in adult MDD due to age differences as this was also more common in unaffected adults compared to adolescents, (b) and that loss of energy may partly be more common in those at high familial risk as this was more common in *adult cases* with a family history of depression. In summary, appetite and weight change and insomnia were more common in adolescents than adults with current MDD and this was robust to sensitivity checks. Loss of energy was also more common in adolescent MDD although elevated familial risk for depression also contributed to this. Loss of concentration was more common in adults and this finding was robust to sensitivity checks.

Depressive symptom profiles in adolescents and adults

Figure 1 illustrates the depressive symptom classes observed in adolescents and adults. In adolescents, three depressive symptom classes were identified: one characterised by low probability of endorsing depressive symptoms (87%), one with high probabilities of endorsing vegetative symptoms of depression (7%) and one with high probabilities of endorsing cognitive symptoms (6%). The highest rates of MDD were seen in the vegetative symptoms class (56%) and these varied by class ($\chi^2(2)=106.60$, $p<0.001$; Figure 1). In adults, four classes were identified: one characterised by low probability of endorsing depressive symptoms (46%; 'low'), one with a high probability of endorsing several symptoms, particularly depressed mood, loss of interest and worthlessness (22%; 'high'), one with a high probability of endorsing depressed mood and worthlessness (19%; 'mood and negative cognitions') and one with a high probability of endorsing anhedonia/loss of interest (14%; 'anhedonia') (Figure 1). Again, rates of MDD varied by class for adults ($\chi^2(3)=149.12$, $p<0.001$), with highest rates in the 'high' class (98%), followed by the 'mood and negative cognitions' and 'anhedonia' classes (39% and 40% respectively) and no cases

in the low symptoms class. Thus, the pattern of co-occurring symptoms associated with the highest probability of MDD in adolescents was one where vegetative symptoms predominated. A profile where vegetative symptoms predominated was not observed in the adult sample.

Discussion

From a clinical perspective, it is useful to consider adult and adolescent depression as the same disorder. Nevertheless, it is accepted that there are aetiological and treatment response differences between adolescent and adult depression. Clinical descriptions of phenomenology in children and adolescents have also highlighted the potential importance of vegetative symptoms in early-onset forms of depression (Goodyer and Cooper, 1993; Nardi et al., 2013; Roberts et al., 1995; Ryan et al., 1987) but detailed systematic descriptions of these symptoms are generally lacking. Moreover, the reliance of these descriptions on clinical samples of young people, collected at different times and from different places using different assessment procedures threatens the external validity of such findings given the 'treatment gap' for adolescent depression, the likelihood of cohort effects and idiosyncratic referral and assessment methods across different sites and settings (Roberts et al., 1995). We attempted to address some of these limitations evident in the current literature by making use of a family cohort where parents and adolescent offspring were assessed repeatedly at the same time point using similar methods.

In a family study which allows 'matching by nature' on a range of confounding factors and where similar assessment and diagnostic protocols for adults and adolescents were employed by the same research team, we found evidence that the presentation of MDD and depressive symptoms differs between adults and adolescents. In a sample of adult and adolescent MDD cases well matched on their overall levels of severity, loss of energy (97%), sleep disturbance - specifically insomnia (87%) and appetite/weight disturbance (87%) were

more common in adolescent than adult MDD (figures were 71%; 63%; 59% for adult MDD).

A similar pattern of findings also emerged for depressive symptoms using latent class analysis. The symptom profile with a high probability of adolescent MDD involved appetite and weight change, insomnia and energy loss at high levels along with low mood.

Conversely, the symptom profile with a high probability of adult MDD was characterised by high levels of all depressive symptoms except weight changes. High levels of low mood and worthlessness were common to adult and adolescent MDD and depressive symptoms. We observed that the vegetative symptoms of insomnia, appetite/weight change, loss of energy were more in adolescent depression and to some extent this distinguishes it from adult depression.

It is recognised that there is substantial phenotypic heterogeneity in depression (Flint and Kendler, 2014). The present findings also indicate phenotypic heterogeneity in the manifestations of depressive symptomatology in adults and adolescents using diagnostic and dimensional approaches to defining depression. Loss of energy was observed in nearly all adolescents with MDD (97%) and at very high levels in the adolescent depression profile associated with the highest probability of MDD. Thus, in this sample of depressed adolescents, loss of energy appeared to be a core depressive symptom. Similar findings have been reported in other studies, for example Ryan and colleagues (1987) reported that fatigue was endorsed as a symptom in over 80% of a clinical sample of depressed children and adolescents. The importance of loss of energy as a 'central' depressive symptom which may trigger or cause other depressive symptoms has been reported in analyses of depressed adults (Fried et al., 2016). The approach used by those authors involved testing whether particular symptoms are especially closely connected to other symptoms in a diagnostic symptom network. It may be that 'central' depressive symptoms like energy loss are particularly important in initial onsets of the depressive syndrome - which often occur in adolescence or early adult life - because they 'activate' other symptoms. Interestingly, sensitivity analyses suggested that loss of energy was also slightly more common in adults

with a history of depression in a parent (although not at the extremely high levels seen in adolescents) suggesting that a familial contribution may also contribute to this result.

Insomnia was also a common feature of adolescent depression (87%). Other studies have also reported that insomnia is present at high levels in youth depression – over 75% in a community sample of depressed adolescent girls (Goodyer and Cooper, 1993) and 88% with sleep disturbance in a US community sample (Roberts et al., 1995). Nonetheless, the present results also showed that insomnia was unlikely to be associated with a high probability of MDD unless also accompanied by other depressive symptoms. This is consistent with previous work using item response theory, showing that sleep disturbance emerged at low levels of depression severity (Cole et al., 2011).

One final finding worthy of comment is that there was no evidence that irritability was more common in adolescent than adult depression despite the allowance of irritable mood as a core mood symptom for children and adolescents in DSM-IV and DSM 5 (APA, 2000, 2013). This finding is consistent with evidence that irritability does not appear to be a 'hallmark' mood criterion for depression in young people and that irritable mood is rare in youth depression without co-occurring depressed mood (Stringaris et al., 2013; Vidal-Ribas et al., 2016). It may instead be that irritability is an antecedent of depression in young people as has been suggested in longitudinal research (Vidal-Ribas et al., 2016). Although we did not specifically examine that possibility in the present study, it has been reported in this sample previously (Rice et al., 2017).

There are several potential reasons for the subtly different manifestations of depression that we observe in adults and adolescents including that depression is not age isomorphic and that there are differences in the symptoms manifested in initial onsets compared to recurrences. Results may also have been influenced by treatment history. Whatever the reason for these differing manifestations, one clinical implication is that not assessing

vegetative symptoms like insomnia, appetite change and energy loss in a young person may result in depression being missed.

The present study has a number of strengths including the use of a community-based family study which controls for a wide range of potential confounds including those that are unmeasured (Sjolander and Zetterqvist, 2017). This coupled with the use of similar standardized assessment and diagnostic protocols for adult and adolescent MDD and depressive symptoms additionally overcomes limitations of existing literature giving greater confidence in the age-related differences in symptomatology observed. The use of a design that circumvents the need for service use in the adolescents is important given the substantial under-treatment of adolescent depression. Nonetheless, the adults in the study were recruited via primary care so a level of treatment seeking was required for the adult sample but adults treated in primary care do not represent a highly selected group. It should be acknowledged that the adult and adolescent samples were recruited in different ways raising the possibility that different sets of bias may operate in the referred adult and community based adolescent sample. One potential limitation is the focus on a group of adolescents with a parent with a history of recurrent depression. It could be argued that the focus on this high-risk group limits the generalizability of findings. Nevertheless, we were able to test this in the sample of adults and found that results were mainly unchanged when comparing to adults with a history of depression in a parent. Moreover, a history of depression in a parent is an extremely common risk factor for adolescent depression with estimates that 40-50% of depressed young people show familial history of MDD in a parent (Lieb et al., 2002). Indeed, the rates of symptom types in the present adolescent MDD sample are extremely similar to those reported in the Oregon community-based adolescent MDD sample (Roberts et al., 1995) giving confidence that the present results are generalizable to adolescent MDD. Another potential limitation is the inclusion of parent reports of adolescent depressive symptomatology on the grounds that parents' evaluations of their children's psychopathology are influenced by their own mental state, with currently

depressed parents reporting more problems in their children. However, evidence illustrates that parents provide reliable and valid reports of their children's motional state irrespective of their own depression with several studies suggesting that depressed parents are especially sensitive reporters of their children's mental health (Lewis et al., 2012; Weissman et al., 1987). Whilst combining reports from parents and the young person themselves is the approach recommended by current UK clinical guidelines we did carry out a sensitivity check using adolescent self-rated symptoms only and found results replicated. The prevalence of MDD was lower in the adolescent than adult sample. This was unavoidable due to the method of recruitment and identification of participants in the study. For the adolescent MDD group, the sample size was relatively small so results require replication. However, results replicated for a continuous measure where sample size of those with depressive symptoms was equivalent in adolescents and adults. Likewise, participants were mostly female although sensitivity checks found no evidence for substantial gender differences. While the methods of assessment and diagnoses were very similar, there were sometimes slight differences in the symptom criteria for the adult and adolescent psychiatric assessments e.g. 'loss of concentration' for adolescents was made up of the items 'inefficient thinking' or 'indecisiveness' but 'loss of concentration' or 'indecisiveness' for adults. Other considerations include that adolescent cases will have been more likely to be first onsets and that the use of a family design will have likely underestimated differences between adult and adolescent depression and so can be considered conservative.

In summary, depression in adolescents differs in presentation to adult depression. Findings suggest that vegetative symptoms are a common presentation in adolescent depression. Given that early treatment remediates the long-term trajectory of adolescent depression, efforts to improve identification, access to brief therapeutic support and signposting for referral to specialist services remain warranted. Results suggest the importance of assessing biological symptoms in young people and are consistent with the aetiology and treatment differences between depression in adults and adolescents.

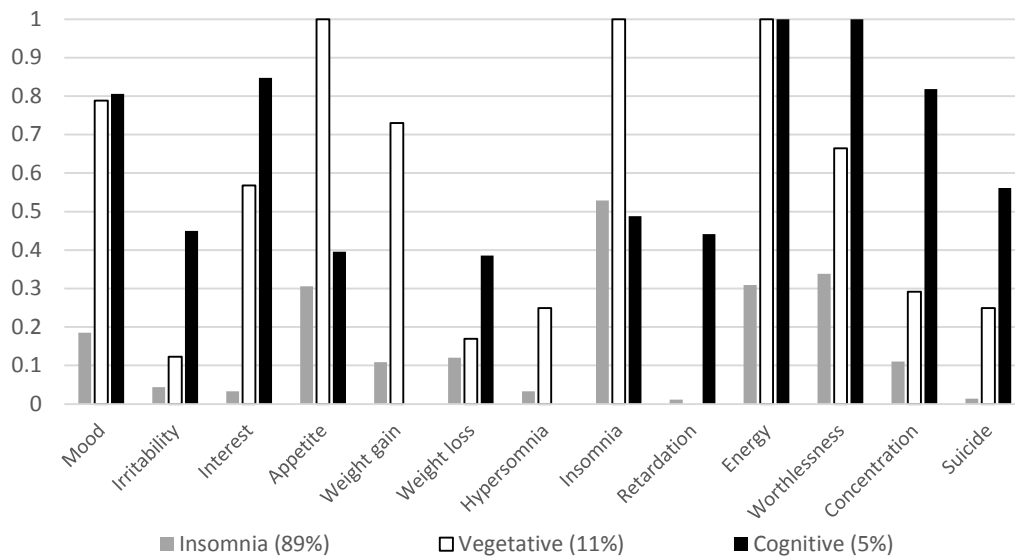
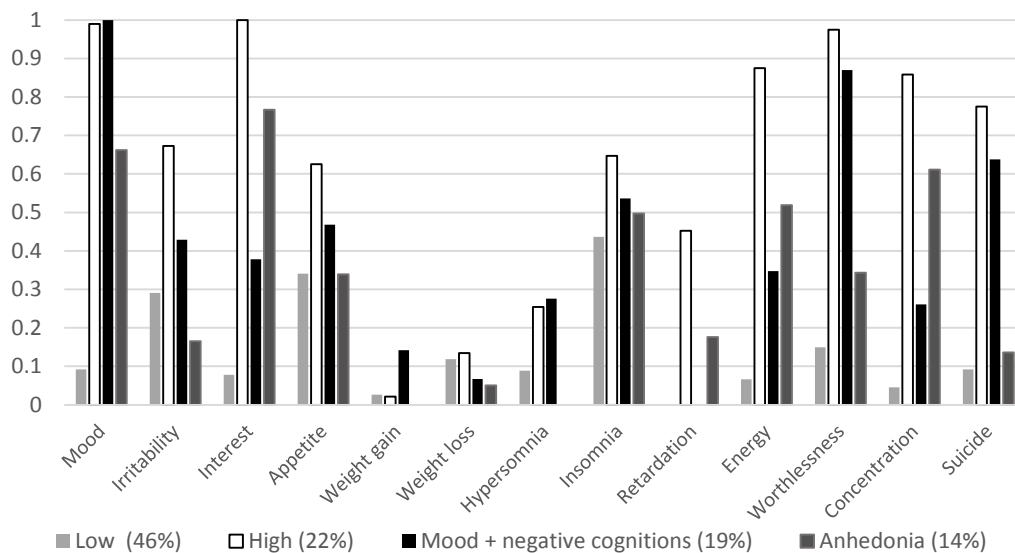
Table 1. Comparing the prevalence of individual depressive symptoms in adolescent and adult MDD

	Percentage of MDD cases		Association with adolescent		
	with symptoms		versus adult MDD		
	Adults	Adolescents	OR (95% CI)	FDR adjusted <i>p</i>	
Core	Depressed mood	98.2	94.6	0.33 (0.04-2.41)	0.33
	Loss of interest/anhedonia	88.1	70.3	0.32 (0.13-0.80)	0.03
	Irritability	46.8	29.7	0.48 (0.22-1.07)	0.11
Vegetative	Change in appetite	56.0	78.4	2.85 (1.20-6.80)	0.03
	Weight gain	3.7	40.5	17.73 (5.37-58.56)	0.0001
	Weight loss	7.4	31.4	5.73 (2.08-15.79)	0.001
	Hypersomnia	22.9	22.9	1.00 (0.40-2.47)	0.99
	Insomnia	63.3	86.5	3.71 (1.34-10.29)	0.02
	Psychomotor retardation	30.3	35.1	1.25 (0.57-2.75)	0.63
	Loss of energy	70.6	97.2	14.55 (1.91-110.76)	0.003
Cognitive	Worthlessness/guilt	85.2	81.1	0.75 (0.28-1.98)	0.63
	Loss of concentration	74.3	38.9	0.22 (0.10-0.49)	0.0007
	Suicidality	65.4	50.0	0.53 (0.25-1.14)	0.14

Table 2. Sensitivity analyses

OR (95% CI)	Original finding (adolescent vs. adult MDD)	Age (unaffected)	Familial risk (adult MDD)	Gender (females only)	Informant (adolescent ratings only)
Loss of interest/anhedonia	0.32 (0.13-0.80)	0.31 (0.14-0.67)	1.47 (0.38-5.72)	0.26 (0.10-0.73)	.10 (.04, .25)
Change in appetite	2.85 (1.20-6.80)	1.27 (0.82-1.96)	1.72 (0.73-4.05)	2.32 (0.91-5.92)	.98 (.46, 2.10)
Weight gain	17.73 (5.37-58.56)	3.10 (1.24-7.76)	0.95 (0.90-1.00)	20.56 (6.00-70.43)	4.33 (1.09, 17.16)
Weight loss	5.73 (2.08-15.79)	1.40 (0.69-2.83)	0.89 (0.83-0.97)	5.33 (1.82-15.59)	4.33 (1.52, 12.31)
Insomnia	3.71 (1.34-10.29)	1.47 (1.00-2.17)	0.81 (0.35-1.88)	5.61 (1.59-19.56)	1.74 (.74, 4.07)
Loss of energy	14.55 (1.91-110.76)	2.76 (1.63-4.67)	2.98 (1.03-8.62)	11.04 (1.43-85.10)	3.33 (1.09, 10.17)
Loss of concentration	0.22 (0.10-0.49)	1.33 (0.70-2.53)	1.77 (0.64-4.88)	0.19 (0.10-0.46)	.13 (.06, .30)

Sensitivity analyses conducted where evidence of a difference in prevalence between adolescent and adult MDD was found

Figure 1 Latent Classes: Adolescents**Latent Classes: Adults**

Footnote to Figure 1: The y axis represents the probability of a depressive symptom being endorsed. For adolescents, the rates of MDD varied by class ($\chi^2(2)=106.60$, $p<0.001$). The probability of MDD is highest in the vegetative class (54%); lowest in the low class (.01%) and intermediate in the cognitive class (29%). For adults, the rates of MDD varied by class ($\chi^2(3)=149.12$, $p<0.001$). The probability of MDD is highest in the high class (97%), lowest in the low class (0%) and intermediate in the mood and negative cognitions (42%) and anhedonia (38%) classes.

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Contributors

AT, AKT and FR obtained funding. AT, AKT, FR, RP and DS supervised the data collection and designed the study. LR, TL and ES performed statistical analyses. AKT provided statistical advice. All authors contributed to writing the manuscript and have approved the final version. FR had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors report no conflicts of interest.

Conflicts of interest

The authors have no conflicts of interest.

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