Cognitive profile partly mediates allergy-associated decrease in mental health

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Abstract

Background

There is a well-established link between allergies and mental health. While both atopic and food allergies are associated with increased levels of depression and anxiety, it is unclear what the mechanism behind this relationship is. Several theories touch upon potential psychological mechanisms, but until now only general reductions in cognitive performance as a function of allergy have been reported.

Methods

We employed a tablet-based high-resolution assessment of cognition that also recorded mental health, socio-economic status, and allergies in 533 children aged 7-9 years. We then employed mediation analyses to investigate the role of cognitive variables in the relation between allergy and mental health, Welch’s t-tests to test for differences between children with and without allergies, and logistic regression to identify what variables predicted allergic state.

Findings

In line with previous research, we found children with allergies reported higher levels of anxiety and depression. Furthermore, they showed a unique profile of higher processing speed, equal verbal short-term memory, and worse performance on tests of fluid reasoning, number sense, search organisation, and spatial short-term memory. We confirmed that these variables predicted allergic state using logistic regression. Finally, mediation analyses showed that cognition partially mediated the relationship between allergy and both anxiety and depression.

Interpretation

Our results suggest that allergies bias children towards particular cognitive profiles, which in turn are risk factors for anxiety and depression. This supports the view that early intervention could reduce the number of allergic children that develops comorbid psychiatric conditions.

Funding

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Research in context

Evidence before this study

It has been known for several decades that children with atopic allergies have an increased likelihood of developing symptoms of depression and anxiety, and more recent work extends this into food allergies. While it was initially thought that poor mental health was a consequence of allergy-induced inflammation, it has since been found that depression can precede allergy. In addition, parallel lines of work have found general decreases in cognitive function as a consequence or cause of atopic allergy.

Added value of this study

Our work adds a precise cognitive mechanism to the literature that illustrates how allergies and mental health interact. We show that children with allergy are more likely to perform worse on various cognitive tasks (e.g. fluid reasoning and spatial short-term memory), but score better on tests of processing speed. These variables also appears in mediation analyses, and predicts allergic state in multivariable logistic regression.

Implications of all the available evidence

Our study suggest that allergies bias children towards a cognitive profile of faster but shallower processing of information, which is known to be a risk factor for anxiety and depression. This provides support for the idea that early intervention in allergic children could prevent the development of comorbid mental health problems, and thereby improve outcomes.
Introduction

There is a well-established link between atopic allergies (e.g. asthma, eczema, rhinitis) and depression (1,2) and anxiety (3). Food allergies have similarly been associated with increased anxiety (4,5), and potentially increased depressive symptoms (6).

While some accounts attribute depressive symptoms to allergy-induced increases in inflammation and immunoglobulin E (IgE) (7), others show instead that depression can induce allergy (8). This aligns with bidirectional theories of mental well-being and inflammation (9). Furthermore, anxiety symptoms are thought to be an unadaptive generalisation of adaptive vigilance for information related to food allergies (10).

Separately from this relationship between allergic responses and mental health, allergies have been associated with poorer cognitive performance in children. Underperformance on cognitive tasks at age 4 predicts atopy at age 6 (11), and children with allergies have poorer cognitive and school outcomes (12). Elsewhere, specific cognitive mechanisms are identified as risk factors for depression in the general population (13). Thus, one possibility is that allergic responses are linked to mental health by predisposing children to a specific cognitive profile rather than through generally decreased cognition.

To answer this question, we employed a broad and precise assessment of cognition in children aged 7-9 years, and recorded both their allergies and sub-clinical symptoms of anxiety and depression.

Methods

We developed a computerised assessment battery that contained well-established tests of number sense, executive function (search organisation) and processing speed, fluid reasoning, inhibition, and spatial and verbal short-term memory. It also contained age-appropriate (spoken) questionnaires for allergies, anxiety, depression, family affluence, and school liking. Participants’ postcodes were obtained from schools or parents to compute their income deprivation affecting children index (IDACI). We have previously demonstrated that our assessments are of good reliability and validity (14), and have described the relationships between measures elsewhere (15).

We collected 468 usable datasets in local schools, and 69 from children who visited our facility (total N=533). They were 7-9 years old, and had a mean z-transformed IDACI of -0.27 (SD=0.92, min=-2.01, max=2.29; higher values indicate higher levels of deprivation). 409 cases were complete, and we used 9-nearest-neighbour imputation on 107 cases with 1 missing value, 15 with 2, 2 with 3, and excluded 4 cases with over 5 (10%) missing values.
Informed consent was obtained from parents and schools, in addition to assent from participating children. The study was approved by the Cambridge Psychology Research Ethics Committee (PRE.2017.102), and conducted in accordance with the Declaration of Helsinki.

In the sample who visited the facility, we could validate the allergy self-report accuracy. Parents but not their children reported an allergy in only 2 cases, and children but not their parents in only 5 cases. A small number of children (7 with parent data; 59 in total) mistook the “other unlisted allergy” for the “no allergy” button, and were not included. In total, 206 children (39% of the sample) indicated they had one or more allergies, which is in line with population estimates (3,16).

Mediation analyses (17) tested the relationship between allergies and mental health, and potential mediation through cognitive variables. We also employed multivariable logistic regression to predict allergic state from socio-economic, mental health, and cognitive variables; using 5-fold cross validation and 3000 bootstrapping iterations to estimate 95% confidence intervals. Simple group differences were computed using Welch’s t-test, which is suitable for groups of different sizes and variances (degrees of freedom are dependent on variance, and thus vary between comparisons).

Role of the funding source

The study sponsors, Templeton World Charity Foundation and UK Medical Research Council, had no involvement in the study design, data collection, analysis, interpretation, writing, or the decision to submit this manuscript for publication.

Results

Allergies significantly predicted higher anxiety \([R=0.11, p=0.008]\) and depression \([R=0.14, p=0.002]\), but cognitive variables partially mediated this (Figure 1) for anxiety \([c'=0.177 (0.089), p=0.046; ab=0.058 (0.013), p<0.001, percentage mediated=24.66\%]\) and depression \([c'=0.155 (0.087), p=0.076; ab=0.121 (0.013), p<0.001, percentage mediated=43.90\%]\). We controlled for socio-economic status (SES; deprivation and affluence) in these analyses, but results were highly similar when we did not.

Besides reporting higher levels of anxiety \([t(410)=2.62, p=0.009, d=0.24]\) and depression \([t(404)=3.11, p=0.002, d=0.28]\), children with allergies (on average) scored poorer on tests of fluid reasoning \([t(367)=3.66, p<0.001, d=0.34]\), number sense \([t(453)=3.78, p<0.001, d=0.33]\), search organisation \([t(453)=2.71, p=0.007, d=0.24]\), and spatial short-term memory \([t(435)=2.32, p=0.021, d=0.21]\). By contrast, children with allergies showed higher average processing speed \([t(526)=-2.56, p=0.011, d=-0.20]\). No differences were observed in school liking \([t(424)=1.95, p=0.052]\), inhibition \([t(440)=0.88, p=0.381]\), and verbal short-term memory \([t(461)=0.11, p=0.911]\). We controlled for SES in these analyses too, but results were again highly similar when we did not.
Figure 1 – Mediation analyses for the relation between allergy (red box) and anxiety (orange box, left panel) and depression (orange box, right panel), with multiple cognitive factors as mediators (yellow boxes). Standardised coefficients and associated p values are reported for each relation, and the total and combined mediation effects are reported in the text below each model. The mental health measures reported here are corrected for socio-economic status (affluence and deprivation), but results are highly similar for uncontrolled outcomes (percentage mediated of 24.97 and 41.93, respectively).

In a logistic regression, variables that did not contribute to predicting allergic state were affluence [β=0.05, CI=[-0.15, 0.27]], deprivation [β=0.18, CI=[-0.02, 0.37]], anxiety [β=0.15, CI=[-0.08, 0.37]], depression [β=0.11, CI=[-0.14,0.36]], school liking [β=0.07, CI=[-0.27, 0.14]], inhibition [β=0.08, CI=[-0.14, 0.30]], and spatial short-term memory [β=-0.12, CI=[-0.35, 0.11]]. Better fluid reasoning [β=-0.25, CI=[-0.5, -0.001]; OR=1.29, CI=[1.00, 1.65]], number sense [β=-0.29, CI=[-0.49, -0.04]; OR=1.30, CI=[1.04, 1.63]], and search organisation [β=-0.22, CI=[-0.43, -0.03]; OR=1.25, CI=[1.03, 1.54]] predicted allergy-free status; while better processing speed [β=0.35, CI=[0.14, 0.58]; OR=1.42, CI=[1.15, 1.78]] and better-than-expected verbal short-term memory [β=0.26, CI=[0.03, 0.50]; OR=1.30, CI=[1.03,1.65]] predicted having any allergy (Figure 2B).
Figure 2 – The top panel (A) shows differences between allergic and non-allergic children on cognitive tasks. Annotated scores are from Welch’s t-tests. The bottom panel (B) shows odds ratios and their 95% confidence intervals computed through 3000 bootstrapping iterations of logistic regression with 5-fold cross-validation. Blue markings indicate predictors of having no allergy, and red of having any allergy. Opaque markings indicate statistically significant predictors (odds ratio confidence interval > 1).
Discussion

Compared to their peers, children with allergies show increased depression and anxiety (even after controlling for SES), and worse fluid reasoning and number sense. However, they showed faster processing speed, and no difference in verbal short-term memory. In essence, children with allergies have quicker processing speed but are less accurate on higher-order cognitive tasks, and this trade-off partly mediates the relationship between allergies and mental health.

Our findings provide a cognitive mechanism that can explain why some reports found allergy onset to precede anxiety (10) or depression (11) symptoms. Specifically, we suggest that having allergies can bias children towards a cognitive profile of faster but shallower processing of information, which in turn is a risk factor for anxiety (18) and depression (13).

There are several theories of how allergy inspires cognitive changes. On a psychological level, adaptive allergy-specific vigilance could bias attention to and interpretation of potentially threatening material (e.g. peanuts or pollen), and thereafter generalise to maladaptive global anxiety (10). Allergy and certain cognitive profiles could also share common biological mechanisms. For example, the G protein-coupled receptor 154 gene is associated with asthma and increased serum IgE, and also with HPA-axis responses to stress and anxiety (11). In addition, being in an atopic state ultimately (through a shift from T helper 1 to 2 responses that produce interleukin-4) affects the serotonin metabolism (2), which is crucial for cognitive flexibility (19,20).

It should be noted that, although no statistically significant direct relationship remains between allergy and depressive symptoms after accounting for cognitive variables, the mediation is only partial. Furthermore, our results are based on cross-sectional data. Hence, our findings support bidirectional causality between allergy and poor mental health (2,8).

One limitation of this study is reliance on children’s self-report. We addressed this by comparing 70 reports from children and their parents, and found 90% overlap. Another limitation is that we did not record whether children were medicated. It is unlikely that the reported specific cognitive trade-off is through a drug confound, because particularly first-generation antihistamines are known to have a general negative rather than a specific impact cognition (12,21). If anything, they would have made allergic children slower.

From a practical point of view, our findings underscore the need for early intervention in children with allergies to counteract potential impacts on cognition. As others have noted, early intervention can improve well-being in both parent and child, improve compliance and outcomes, and reduce mortality (22).
Conclusion

Allergy-associated increases in depression and anxiety symptoms are mediated by a cognitive trade-off: Children with allergies are more likely to process information faster, while their peers without allergies process at greater depth. Accounting for cognitive differences diminishes the relationship between allergic state and mental health, highlighting cognition's central role in allergy-associated changes in mental health. Our findings highlight the need for early intervention to prevent allergy-induced changes in cognition to take hold, and thereby improve clinical outcomes.

Declaration of interests

The authors declare that there are no relevant financial or personal relationships that could be conceived as actual or potential conflicts of interests affecting the analysis, interpretation, or publication of the current study.

Data sharing

The authors will make a synthetic dataset available with the publication of this manuscript, as well as the analysis code via GitHub (https://github.com/esdalmaijer/). It will be constructed to match the properties of the original data (using R package synthpop), without the danger of potential deanonymisation of participants. The original data will be available from the corresponding author upon request, and upon signing an agreement to not publicly share it. This ensures that our analyses are reproducible, while maintaining the privacy of our participants.
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