Identifying neurobehavioural symptom groups based on shared brain mechanisms

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Aim

- ◆ To investigate whether symptoms contributing to DSMV/ICD10 diagnoses can be reconfigured to identify 'neurobehavioral' symptom groups that best represent specific underlying dysfunctional brain networks in adolescence

Abstract

- ◆ Most psychopathological disorder develops in adolescence. The biological basis for this development is poorly understood.
- ◆ To enhance diagnostic characterisation, and develop improved targeted interventions, it is critical to identify behavioural symptom groups that share neural substrates.
- ◆ We ran analyses to find relations between behavioral symptoms, and neuroimaging measures of brain structure and function in adolescence.
- ◆ We found two symptom groups, consisting of anxiety/depression and executive dysfunction symptoms respectively, which correlated with distinct sets of brain regions and inter-regional connections, measured by structural and functional neuroimaging modalities. We found that the neural correlates of these symptom groups were present before behavioural symptoms had developed.
- ◆ These neural correlates showed case-control differences in corresponding psychiatric disorders, depression and ADHD, in independent clinical samples.
- ◆ By characterising behavioral symptom groups based on shared neural mechanisms, our results provide a framework for developing a classification system for psychiatric illness, which is based on quantitative neurobehavioural measures.

Results

Figure 1: Results of the first msCCA-regression analysis showing relations between anxiety/depression psychiatric symptoms and neuroimaging measures in the IMAGEN sample. (a): The full msCCA-regression model linking psychiatric symptoms to VBM, TBSS and rs-fcMRI neuroimaging measures at age 19. We found associations between psychiatric symptoms and neuroimaging measures of $r = 0.59$ ($p < 0.001$) in the training set, and associations between symptoms and the brain of $r = 0.23$ ($p < 0.001$) in the test set; (b): Shows the msCCA-regression model linking psychiatric symptoms with the different neuroimaging measures (c): Psychiatric symptoms contributing to this relation are shown on the left, their canonical weights are shown in red. (d): rs-fcMRI measures of functional connectivity. (e): VBM measures of grey matter volume associated with symptoms. (f): TBSS measures of fractional anisotropy (FA).

Figure 2: Results of the second msCCA-regression analyses showing relations between executive dysfunction symptoms and neuroimaging measures in the IMAGEN sample, following the removal of the first canonical relation. (a): The full msCCA-regression model linking psychiatric symptoms to VBM, TBSS and rs-fcMRI neuroimaging measures at age 19. We found associations between executive dysfunction symptoms and neuroimaging measures of $r = 0.46$ ($p = 0.004$) in the training set, and associations between symptoms and the brain of $r = 0.19$ ($p = 0.002$) in the test set; (b) msCCA-regression model linking psychiatric symptoms with the different neuroimaging measures (c) Symptoms contributing to this relation are shown on the left, their canonical weights are shown in red. (d) Rs-fcMRI measures of functional connectivity. (e) VBM measures of grey matter volume associated with symptoms. (f): TBSS measures of fractional anisotropy (FA).

Figure 3: Longitudinal analysis of canonical correlates. (A) anxiety/depression symptom correlates: VBM and TBSS brain correlates established at age 19 are associated with anxiety/depression behavioural symptoms at age 19, but not at age 14. Brain correlates at 14 years predict the manifestation of behavioural symptoms at 19 years. (B) Executive dysfunction symptom correlates: VBM and TBSS correlates established at age 19 are associated with behavioural symptoms at age 19, but not at age 14. Brain correlates at 14 years do not predict the manifestation of behavioural symptoms at 19 years.

Figure 4: Differences in the grey matter correlates of anxiety/depression and executive dysfunction psychiatric symptoms, between cases and controls for a range of psychiatric illnesses. For the box and whisker plots, the central mark in each box represents the median, with the top and bottom edges of the box indicating the 25th and 75th percentiles of the sample respectively. (a): Differences in grey matter volume between patients and controls in the anxiety/depression set of grey matter correlates are shown in the left-hand panel. The effect sizes (calculated using Cohen's D) relating to these differences are shown in the right-hand panel. (b): Differences in grey matter volume between patients and controls in the executive dysfunction set of grey matter correlates. The effect sizes (calculated using Cohen's D) relating to these differences are shown in the right-hand panel. For display purposes, total grey matter in each case-control comparison is divided by the pooled standard deviation.

Conclusion

- ◆ By basing symptom groups upon brain correlates, and by demonstrating specific associations of these correlates with clinical psychopathology, we have characterized stratification markers based on shared neural substrates. By discovering that these brain correlates identified in young adults are already established during adolescence, we have characterized biological risk markers prior to the manifestation of symptoms. Our work thus shows how major obstacles can be overcome in developing a taxonomy for psychiatric illness based on quantifiable neurobehavioral phenotypes.