

Cognitive and Social Profiling- Exploring Rasopathies (CASPER) study summary

The aim of the CASPER study was to study the learning and behavioural problems in children with Noonan syndrome, Cardio-fascio-cutaneous (CFC) syndrome and Costello syndrome. We particularly wanted to study whether children with these conditions were more likely to show symptoms of Autism Spectrum Disorder (ASD) or Attention Deficit Hyperactivity Disorder (ADHD).

Fifty children and families participated in this study. Of these, 40 children had Noonan syndrome, 9 had CFC and 1 had Costello syndrome. The study was advertised via the Noonan syndrome /CFC/Costello charities and the regional genetics service in Manchester. Families interested in the study were asked to get in touch with the research team. All the research assessments were carried out in the family's homes by two researchers. A thorough battery of tests was used to understand the behavioural difficulties experienced by these children and families. The tests included parent interviews, young person assessments and reports from school. Since there was only 1 participant with Costello syndrome, these results are not reported.

The results from the CASPER study are as follows:

Noonan syndrome

40 children (25 males and 15 females) with NS syndrome were assessed. The mean age of the children was 10 years and 10 months. Of these, 16 children had a Statement of Special Educational Needs. Three children had a pre-existing diagnosis of ASD and 1 child had a diagnosis of ADHD. The mean overall IQ was 87 (range 61-120); 3 children had full-scale IQ below 70.

The ASD assessment was carried out using Autism Diagnostic Interview-Revised (ADI-R) for parent interview and the Autism Diagnostic Observation Schedule (ADOS) for child observation. Using standardised criteria, 12 children (10 males, 2 females) with Noonan syndrome met the criteria for ASD, 12 children (8 males, 4 females) had some symptoms of ASD and 16 children (7 males, 9 females) were non-ASD. Males were much more likely to meet the criteria for ASD than females.

The ADHD assessment was carried out using parent-reported Conners questionnaire, researcher observation and assessment. Using a combination of these measures, 21 children (52.5%) were rated to have significant symptoms of ADHD.

CFC

9 children (5 males, 4 females) with CFC were assessed. The mean age of the CFC group was 10 years, 1 month. Of these, 8 children had a Special Educational Needs (SEN) Statement. None of the children had a pre-existing diagnosis of ASD or ADHD. Using standardized instrument (Wechsler's Abbreviated Scale of Intelligence), the mean overall IQ in 6 children with CFC was 73.9 (range 45-100). In 3 children with significant learning difficulties, the IQ was measured using the Mullen Scale of Early Learning.

On the ASD assessment, 8 children (88.9%, 4 males and 4 females) met the criteria for ASD and 1 child had some symptoms of ASD. On the ADHD assessment, all of the participants were rated as having significant symptoms of ADHD.

Summary of the results and conclusions

This is the first systematic study to confirm a high prevalence of ASD and ADHD in Noonan Syndrome and CFC. In Noonan syndrome, 30% of children were found to have ASD and 52% children were found to have ADHD. Boys with Noonan syndrome were much more likely to have ASD than girls. In the CFC group, almost all the children we studied were found to have significant ASD and ADHD.

The high prevalence of ASD and ADHD has important implications for clinical management and educational planning. The data on pre-existing diagnosis makes it clear that ASD and ADHD are under-recognised in children with Noonan syndrome and CFC possibly due to 'diagnostic overshadowing', where the behavioural difficulties are ascribed to the genetic diagnosis itself. Our findings suggest that screening for ASD and ADHD should be undertaken in all children with NS and CFC, and that these developmental disorders should be considered as part of the differential diagnoses when children present in the clinic with problems of behaviour, social adjustment or relationships.