

Families for Families Day - 23rd April 2016

Professor Jonathan Green presentation

Thanks for the invitation. It's a pleasure to be here to talk to you. Some of you here last year heard other members of my team talk about some of this work but I guess there'll be some people who weren't here last year so I'm hoping it'll be new, and also I'm going to make this a little bit more clinical so I'm going to focus a little bit more on treatments availability and things like that. And of course that will also play into the Q&A this afternoon so if there are things which come up from my talk that you'd like to follow up on then please talk to me over lunch or bring it up in the Q&A in the afternoon.

So I'm a Child & Adolescent Psychiatrist working in Manchester and that means I'm interested in the thinking, the feeling and the behaviour of children as they develop and grow; and also in their family context. And over the last few years we got very interested in trying to understand some of the particular problems in thinking, feeling and behaviour that occur in children with a number of different developmental disorders including the Rasopathies. So this is an example of our work applied to Noonan Syndrome and I'm also going to make reference to our work which has been similar with NF1, another Rasopathy, and you will see that also we've worked with CFC in this group as well.

So, why to do this? Well, partly it's very clear from talking to families that problems with children's behaviour are uppermost in many families' minds with children growing up with Noonan Syndrome. So talking to Mums and Dads about their concerns when we went to their homes to do assessments, most of them were worried about behavioural issues and obviously the medical issues were also important and so were learning and academic ones. Why did we think it was useful to investigate this? Well, trying to understand the nature of these behavioural and mental health problems in conditions like Noonan Syndrome is important and it's useful; and one of the key reasons for looking at it in the way that we do, is that in the past, it's often been the case that people have looked at the behavioural aspects in Noonan Syndrome and similar syndromes like it, and thought that the behavioural problems that are being seen in the children are really just part and parcel of the syndrome – it's like “well, your child's got Noonan Syndrome so I'm afraid that goes with the territory in that they have problems like this.” We take a rather different approach. Noonan Syndrome is defined by a particular variation in the genome – a genetic condition – but that doesn't necessarily mean that that explains the behaviour in its own right or that actually we don't need to look at the behaviour as a separate and particular type of thing. And we call this problem Diagnostic Overshadowing. In other words, you know that the child has NS so you think that everything else is explained by it. One of the things we're trying to identify is that this is not necessarily the best way to look at this. We can look at these behavioural and mental health problems in their own right and make some understanding based on that. Partly that's important because there are specific treatments available for many

of these problems in many many children and so there's remediation available. It's also helpful in education and other planning so when you're trying to understand your child and help other people understand the child, then these kinds of things are useful. And it's not that there's something special about Noonan Syndrome or Rasopathies in this. Most children with most neuro-developmental conditions do have an increased risk of behavioural or mental health problems. So this isn't that there's something special about NS; this is a general issue in children whose development generally, particularly their brain development, is happening in a slightly different way to other children. The reasons why they are at risk because of that are very interesting – I'm not going to go into that at this point – but that gives us a lot of very interesting theoretical research insights into what the fundamental nature of these problems is in the first place. But I want to emphasise this isn't specific to Noonan Syndrome – this is a very general phenomenon.

So what we did in the CASPER Study, is that we did an in depth assessment of 50 children with Noonan Syndrome and CFC mainly and one case of Costello as well, from the point of view of thinking, feeling and behaving. We did it at home – our researchers went to visit families at home and some of you may have been part of the study. We looked at 30 boys and 20 girls in what we call their middle childhood – they were all around 10 years of age. So what I'm speaking about here applies to children rather than adults or even older children – it's not necessarily generalised. It's children growing up.

The first thing to say is that we looked at the IQ – the intelligence quotient – the cognitive learning ability generally of the families, and one of the characteristics of Noonan Syndrome in which it's similar to Neurofibromatosis is that the IQ profile is very slightly, not hugely, but slightly shifted. In other words, there is some compromise of general learning ability in this group but it's not a huge one. We don't call this a very severe problem, whereas in CFC the compromise in learning difficulties is much greater.

So I'm going to run through a number of the particular behavioural and mental health problems that we looked for in our group of 50 children just to give you an idea of the sort of things children with NS might come up against.

The first one is ASD which stands for Autism Spectrum Disorder. I'm sure you've heard about Autism as a condition. There's a new TV drama based around it. It's called "The A Word" which gives a really good insight to the impact of Autism on families. ASD is an important condition – about 1% of the general population of children are affected with ASD but most of the Autism that we see in the community is what we call idiopathic – it's the consequence of genetic variation in a lot of different genes in a very non-specific way. But there are varieties of Autism that are caused by single gene problems or specific gene abnormalities that we know about and that of course is the case with Noonan Syndrome. So in this kind of case we talk about what we call Syndromic Autisms - that is Autism caused by a particular problem.

And these are the sort of things you see in Autism:

- difficulties with social communication, both understanding and expressing socially
- difficulty in developing and maintaining relationships
- and then another cluster of difficulties that children with Autism have, which is what we call restrictive and repetitive behaviours – these are rigidities or behaviours which have to be repeated, fixed routines, activity which often can be quite difficult to manage in family life.

And we looked at ASD in the sample in a rather in-depth and rigorous way by talking directly to the children and interacting with the children and also talking to their parents. It was quite a sophisticated assessment.

These are the sorts of things that parents of children with Autism often report and find difficult and some of you may recognise these:

- routines
- lack of or difficulty in conversations and with relationships
- repeating unusual phrases
- difficulty with eye contact and social interaction
- intense interests etc and
- some difficulties with processing sensory information, so real sensitivity to noises or lights and things like this.

So what did we find? Well, this is in the group as a whole, for Noonan Syndrome what we find is that 30% of our sample – and remember, this is a sample which we can't say is representative of everyone with Noonan Syndrome in the country, it's quite a rare disorder so we had to actively get referrals and cases so we can't be sure that this is representative but nevertheless this is what we find in a sample of 50 and it's probably a pretty good indication of what's generally out there, so 30% - that's almost a third of these children had patterns of behaviour that we could define as Autism or Autistic Spectrum Disorders; and another third had partial features. So these are features that don't meet the full criteria but show little bits of it as it were. So that's over half the children had difficulties of this kind so it's very striking. It's rather similar, slightly higher but rather similar to what we find in Neurofibromatosis and in some other neuro-developmental conditions but nevertheless this is a high proportion. The boys are more at risk of this than the girls – there's a 5:1 ratio and that's true generally through the population that Autism is more common in boys. So a high proportion. In the CFC group, it's almost universal – it was a small group – it's only 9 children we looked at but almost all of them had indicators of this kind.

So this is an important prevalent problem to look out for and it can explain a lot of difficulties which children are having in family life and at school and in their social environment.

The moderate news is that there is no magic cure for Autism. This is a developmental problem that we have no way of making go away in any magical way. But the more positive news is that there are many things we can do to alleviate the difficulties and many of us in my profession have been working very

hard over many years to develop good treatments for Autism in development. And we're making pretty good progress I would say.

So there are treatments available. The most well evidenced treatments recommended by NICE and these bodies that assess treatment evidence – the most evidence based treatment that we have at the moment for the core symptoms I've been talking about are these social communication treatments. These are interventions that usually work through the parents but can also work directly with the child to enhance social skill and social communication. And we've developed one of these social communication interventions in Manchester which has been quite extensively tested now and it shows good effects in improving the child's social communication in the family and also reducing the number and extent and severity of Autism symptoms. And our particular kind of work that we do works with parents using video feedback to help parents to understand more about the social communication of the children and to help them respond in an appropriate way. It has a beneficial effect on the children.

But there are lots of other things that can be done – social skills support particularly in schools, techniques such as so called social stories which are very effective ways of helping a child with Autism to plan their responses in particular situations. These can all be useful.

The diagnosis of Autism is very helpful in educational planning. It alerts Education Authorities and schools to the special needs of the child in this particular regard. It can attract additional resource for additional help, for teaching assistants and learning support assistants in schools, and if necessary there are some specialist units for Autism available for children generally which children can be eligible for which are particularly adapted for working this group. So there are lots of good reasons to understand and to identify this kind of problem in children generally and children with Noonan Syndrome. So that's ASD.

Now I want to talk about Attention and Hyperactivity so this is so-called ADHD which I'm sure many of you will have heard of - Attention Deficit Hyperactivity Disorder. And again this a neuro-developmental disorder generally which is not uncommon at all in the general population – so up to around 4% of children in the general population have these kinds of difficulties but they are more common than that in children with atypical development who are struggling in one way or another. One of the difficulties that manifests in this problem is inattention so the child can't keep focused on things very well, has trouble paying attention, difficulty in self organising. And then there are a range of difficulties in behaviour to do with hyperactivity – constantly on the go, can't stop, like running with a motor – I see some nods and smiles with people recognising this, and impulsivity which means you just act before you think, so bang you're off and often get yourself into trouble. So there's a general sense of recognition in the room – examples of behaviour you're probably familiar with, many of you – difficulties sitting down, staying still, hard to listen and attend for a long time, flipping away in their attention, interrupting, forgetting, not organising, difficulty to keep on task, constant chatter. So these are the sorts of things that parents talk about with this

kind of disorder. Now of course lots of kids show problems of that kind as they grow and gradually they how to manage their own behaviour and their impulses etc but the thing about ADHD is that partly it's very extreme and it also doesn't improve in the way that regular kids do in development so this is a sustained difficulty of this kind. And we know quite a lot about the neurological difficulties which underlie this in some children. OK, so what do we find in Noonan Syndrome? Well, what we find is about half of the kids in our sample of 50 suffered from ADHD. This is at a diagnostic level so a significant rate and almost all the kids, 90% of kids with CFC have this problem. So this is pretty significant and only one child with Costello was assessed in the study so we can't really say much about that. So this is pretty prevalent again.

Some of these kids with ADHD have Autism so there can be an overlap but generally that's not the case – they have one or the other. Again identifying this problem is useful, partly so you can understand the nature of the difficulties for the child and make a bit of sense of that behaviour but also because there are treatments available for this that can make a big difference. And we have a lot of good evidence-based treatments to help with ADHD. The most immediately effective thing that helps with all aspects of ADHD are a range of medications that have been developed – so called stimulants. It seems odd that you should have a child that's buzzing round all the time and that stimulants help but that actually the way this class of medicines called stimulants work on the brain actually helps the child to get more control over their behaviour and it improves their attentions, slows their behaviours down and makes them less compulsive. So there are a range of medications which are very effective. Not all parents want their child to be on medication and we as doctors don't want children to be over-medicated for this kind of problem but there's no doubt that when you really need it that they are effective but there are other things that can be done so there are a lot of parental support and behavioural techniques which aren't really as effective in reducing the ADHD itself but can certainly help families manage the condition.

As with Autism, identification of ADHD is extremely useful in educational planning to help schools and education authorities understand what the child's up against in development and to access resource on occasion. So that's ADHD.

The another thing that came up very strongly in our study in relation to Noonan Syndrome was difficulties with behaviour, aggressiveness or what we call oppositionality – constantly just being anti and difficult to fit in with other people's routines etc and finding it difficult to comply with rules and talking back etc. Oppositional behaviours are very common and aggression as well on occasions and this is of course distressing – it's disruptive for families, difficult and it can cause a lot of heartache for both families and children. We saw rather a lot of this in the sample. So about 40% overall showed some level of these difficulties and about two thirds of the participants in the study talked about their children exhibiting a level of aggression in the family but rather less outside and that's very common that children tend to be more disruptive/aggressive in the home where it's familiar than outside. So this is a significant issue. We wanted to understand why, because aggression as a behaviour, oppositionality as a

behaviour, isn't just a thing in itself, it's a symptom of something else. We need to understand "well, why is that? Is it that the child has a teacher who doesn't understand them? Is it that they are being bullied? Is it because they are distressed in some way?" There are a lot of reasons why a child can get aggressive and oppositional and we usually try to find the underlying cause. We couldn't look at everything because we didn't measure everything but in terms of what we measured, we came up with quite an interesting finding which was if we looked at these aggressive behaviours, there are two things which stood out and which seemed most associated with them. One was whether the child had problems with ADHD and the other was whether they had problems with anxiety – and I'm going to come on to anxiety later. So in terms of an underlying problem from these, these two problems seemed to be rather important. The ASD in itself, the Autism in itself, didn't contribute very much which was quite interesting; so the main problem related to that and you can understand that a child who's very impulsive, who's very active all the time, getting into trouble all the time, can't listen, that this generates oppositional and difficult behaviour in families and school and this is very common. Well there are treatments – I've already talked about some of the treatments for ADHD, I'm going to talk about treatments for anxiety, and there are ways in which we can help parents manage oppositional and aggressive behaviour in the professional realm, techniques that can be used. But there's no getting away, this can be a very difficult issue but with really understanding it and adjustment and the appropriate support you can usually make a lot of difference to these kinds of aggressive problems. In extremis, when the aggression's really uncontrolled and uncontrollable, there are some medications that we can use which can help.

Social functioning. Well, this is a general issue so this is not Autism as such but children who just find it difficult to get along on social life and at school, problems with friendships, difficulties in understanding and reacting. Obviously this is part and parcel of the ASD but also occurs more widely than that and we looked at social functions – it's such an important aspect of children's development – families and children. Well, there were lots of difficulties, you won't be surprised to see this by now so half the sample, parents felt [their child] didn't really know how to make friends – really distressing for parents when they see that. And over two thirds had trouble keeping friends, and you'll see that we did a test of facial recognition. This is a more cognitive thing that we do which I won't talk about very much today but some of the children did have difficulty – basically social understanding of the facial expressions of others which is one of the problems which can often underlie this. What caused the social functioning difficulties? Well, here's another interesting thing. Again it was the ADHD that seemed to be mostly associated so So ADHD is a very disruptive kind of problem socially. It makes a big difference in a social group. If you're in the playground as a little child, you'll know what a tough place the playground can be with your peers and you're coming in and you don't know how to join a group. Maybe you barge in and you get them all worked up and you start hitting people instead of negotiating stuff – that gets you into trouble very quick. And that's the sort of problem that we

think that underlies a lot of the social functioning here. It relates to the ADHD. Of course these two things also contribute.

And finally I just want to talk a bit about anxiety. So here's a feeling problem. Of course all children get anxious at times; you know that's normal to be the case. It's true for adults as well. But what we think of as more problematic anxieties - a child who's always anxious about things that really they don't need to be anxious about, it really affects their behaviour; it means they can't separate or go out with confidence into the world and they worry a lot. So this is the sort of thing we're interested in. And, well, we found a fair amount of anxiety in this sample. So around 10% of the Noonans had lots of anxiety; so it's not as high as some of the other things we've seen but about a third had little bits of anxiety. The rates were slightly higher in CFC. So this isn't a massive issue but it's certainly higher than you'd get in the regular population. And there are lots of good treatments for anxiety. We're very good at treating anxiety in children, primarily through psychological treatments which are usually very effective if they're done well, and so-called cognitive behaviour therapy and other behavioural therapies are very effective. And if these don't work then we've got a range of medicines that we can also use for children with anxiety. So treatments available. Probably a lot of you are saying to yourselves "oh, it's very well him saying that. I can't get access to someone who's really going to help me". I bet we have questions about that. And it is true that nationally the availability of treatments and help of this kind through child mental health services is not as good as it should be and that's a shortfall that is a national ...well I call it a national disgrace because it's my area and I feel passionately about it but it is definitely a big big problem. And that's a national issue, so there are difficulties in accessing appropriate treatments. We are working in the profession as hard as we can to make things more available but what you need to know as parents is these things are available in theory, they're there. It can be done. There's help available for these problems.

So that's all I'd like to say and just thanks to the Newlife Foundation who supported this work which was extremely helpful, to Mike Patton, and to my team and colleagues in Manchester Clinical Genetics who all worked with us together on this project, so I appreciate your attention, thank you.