Social Competence and Social Information Processing in Children with Neurofibromatosis Type 1

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This dissertation is presented for the degree of Master of Philosophy (Psychology) at Macquarie University.

Submitted

December 2015

Revised

May 2016

DECLARATION

I hereby certify that the work in this dissertation, entitled "Social Competence and Social Information Processing in Children with Neurofibromatosis Type 1", has not been previously submitted for a degree at Macquarie University or any other institution.

I also certify that this dissertation contains only original pieces of research written by me. Any assistance received in conducting the research and/or preparing the thesis has been appropriately acknowledged.

This research was approved by the Children's Hospital at Westmead Human Ethics Committee (reference number 10/CHW/43) and the Macquarie University Ethics Committee.

Signed:

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ACKNOWLEDGMENTS

Firstly, I would like to thank my brilliant supervisors: Associate Professor Melanie Porter, for her generosity with her time and extensive knowledge which made this dissertation possible; Dr Jonathan Payne, for sharing his expertise in neurofibromatosis type 1 and patiently guiding me through the complexities of research design; and Dr Tracey Williams, for her efficiency, wisdom and frequent motivational pep talks. I would also like to express my sincere appreciation to Ms Samantha Bzishvili for her assistance with data collection and to Dr Naomi Sweller for sharing her statistical expertise.

Thanks must also go to the wonderful staff at the NF1 Learning Disorders Clinic for sharing both their knowledge and their workspace with me. I would also like to thank the children (and parents) who participated in my research for their enthusiasm, proactivity and flexibility.

Finally, I would like to thank my family and friends for their unwavering love and patience as I undertook this challenging and time-consuming project. I have greatly appreciated their many forms of support, which have included backrubs, cups of tea and coffee, patiently listening to long rants about data analysis and, of course, pretending to be interested.

DISSERTATION ABSTRACT

This thesis investigates social competence and social information processing in children with neurofibromatosis type 1 (NF1). The aims of this thesis were threefold: 1) to investigate day to day social competence in children with NF1 (Paper 1), 2) to better understand facial emotion recognition abilities in children with NF1 (Paper 2) and 3) to explore face perception and attention to faces in children with NF1 (Papers 2 and 3). In relation to the first aim, the results of Paper 1 indicated that, as a group, children with NF1 displayed significantly poorer day to day social competence than their typically developing peers. Children with NF1 who displayed high levels of autistic symptomatology and socially anxious behaviour were particularly at risk of social competence problems. Pertaining to the second aim, the findings of Paper 2 suggested that children with NF1 displayed poorer recognition of threatening emotions, but not non-threatening emotions, compared to typically developing children. Children with NF1 displayed particular deficits in identifying fear, but also had difficulty identifying anger. Facial emotion recognition problems were not significantly related to the manner in which children with NF1 viewed faces or their ability to perceive and discriminate between faces, although a non-significant trend was observed whereby poorer face perception skills were associated with reduced proficiency in identifying anger. In relation to the third aim, results suggested that children with NF1 spent less time attending to faces than typically developing children both when presented in isolation (Paper 2) and when presented in the context of a static social scene (Paper 3). As a group, children with NF1 also displayed significantly poorer face perception abilities than typically developing children (Papers 2 and 3). Taken together, these findings indicate that children with NF1 are at significant risk of day to day social competence problems. Moreover, findings indicate that impairments in perceiving, interpreting, and attending to information from faces may be important aspects of the social-cognitive phenotype of NF1.

GENERAL INTRODUCTION

The population of interest in the present thesis is children with NF1. NF1 is an autosomal dominant genetic disorder with an estimated prevalence of 1 in 3,000. The disorder is associated with distinctive physical characteristics, which include skinfold freckling, café-au-lait macules (pigmented birthmarks) and neurofibromas (benign nerve sheath tumours) (Williams et al., 2009). While there is considerable variability in the clinical presentation of children with NF1 (Szudek, Birch, Riccardi, Evans, & Friedman, 2000), common complications of the condition include neuroanatomical abnormalities (Payne, Moharir, Webster, & North, 2010), specific cognitive impairments (Hyman, Shores, & North, 2005; Huijbregts & De Sonneville, 2011) and a high prevalence of psychological comorbidities (Garg, Lehtonen, et al., 2013; Johnson, Saal, Lovell, & Schorry, 1999).

NF1 is associated with a variety of structural neurological abnormalities. Focal T2 hyperintensities (high intensity lesions on T2-weighted MRI images) occur in up to 90% of paediatric patients with NF1 (Gill, Hyman, Steinberg, & North, 2006). These anomalies are most frequently observed in the cerebellum, basal ganglia, thalamus, brainstem and hippocampus (Lopes Ferraz Filho et al., 2008). Additionally, as many as 50% of children with NF1 have an unusually large head size (head circumference > 95^{th} percentile) (Van Es, North, McHugh, & De Silva, 1996), which is accompanied by an increase in total brain volume, known as megalencephaly (Cutting et al., 2002). Specifically, neuroimaging studies have revealed increased frontal white matter volumes in individuals with NF1, which might underlie some of the cognitive problems commonly seen in this population (Cutting et al., 2002; Greenwood et al., 2005). Nevertheless, investigations into the relationships between neuroanatomical abnormalities and specific cognitive impairments in individuals with NF1 have yielded inconsistent findings at best and, as such, the impact of neuroanatomical abnormalities on cognitive functioning in NF1 remains unclear (Payne et al., 2010).

Functional neurological abnormalities (that is, dysfunctional neural networks) have also been identified in individuals with NF1. For example, Billingsley et al. (2004) used functional magnetic resonance imaging (fMRI) techniques to investigate the neural basis of visuoperception in NF1 and found greater left than right hemisphere activation in NF1 participants during a visuospatial judgment task, while controls showed the reverse pattern. Additionally, in a recent study, Loitfelder et al. (2015) used resting-state scanning methods to investigate functional connectivity between brain regions commonly associated with executive and social functioning (the ventral anterior cingulate cortex, amygdala, orbitofrontal frontal cortex and posterior cingulate cortex) in children with NF1. The authors found that children with NF1 displayed differences in functional connectivity between a number of brain regions, including between the left amygdala and the frontal cortex, insula, supramarginal gyrus and posterior cingulate cortex, compared to healthy controls. Taken together, these findings indicate dysfunctional neural networks in NF1 which might underlie some of the commonly observed cognitive and social difficulties in this population.

Cognitive impairment is commonly reported in NF1, with specific cognitive deficits evident in attention, language, visuospatial skills and executive function (including planning, organisation, inhibition, and self-monitoring) (e.g. Hyman et al., 2005; Lehtonen, Howie, Tump, & Huson, 2013; Payne, Hyman, Shores, & North, 2011; Rowbotham, Pit-ten Cate, Sonuga-Barke, & Huijbregts, 2009). Intellectual functioning falls broadly within the normal range, although a downward shift in overall intelligence levels (compared with the general population) has been reported (Feldmann, Denecke, Grenzebach, Schuierer, & Weglage, 2003; Ferner, Hughes, & Weinman, 1996; Hyman et al., 2005). Academic difficulties are also common, with between 50 and 70% of children with NF1 demonstrating impairments in literacy and numeracy skills (Brewer, Moore, & Hiscock, 1997; Hyman, Shores, & North,

2006) and approximately 20% estimated to meet criteria for a specific learning disability (Hyman et al., 2006).

Children with NF1 also display higher rates of comorbid psychopathology compared to the general population. The NF1 population prevalence of Attention Deficit Hyperactivity Disorder (ADHD) is estimated to fall between 30 and 50% (Hofman, Harris, Bryan, & Denckla, 1994; Hyman et al., 2005; Mautner, Kluwe, Thakker, & Leark, 2002) and approximately 25% are estimated to meet criteria for Autism Spectrum Disorder (ASD; Garg, Green, et al., 2013). Additionally, there is evidence to suggest a predisposition towards anxiety disorders in children with NF1, with a recent study showing that children and adolescents with NF1 display significantly higher levels of anxiety symptomatology on a self-report measure compared to healthy controls (Pasini et al., 2012). It is assumed that the high rates of developmental psychopathology documented in NF1 are related in some way to a direct effect of the NF1 gene on brain structure and/or function, although the exact nature of this relationship remains unknown (Garg, Lehtonen, et al., 2013).

Regardless of the presence or absence of comorbid psychopathology, individuals with NF1 are also reported to display significant deficits in social functioning. Anecdotally, reports from children with NF1 and their parents suggest that they are often teased and rejected by their peers and have difficulty forming and maintaining friendships. In keeping with these observations, informant ratings of socio-emotional functioning in children with NF1 suggest a high incidence of behavioural and peer-related problems in this population, including distractibility, hyperactivity, shyness and awkwardness (Barton & North, 2004; Descheemaeker et al., 2005; Dilts et al., 1996; Huijbregts & De Sonneville, 2011). Children with NF1 are also reported to display reduced accuracy and efficiency in processing social information, with a recent study identifying deficits in both face recognition and facial emotion recognition abilities in children and adolescents with NF1 compared to their typically

developing peers (Huijbregts, Jahja, De Sonneville, De Breij, & Swaab-Barneveld, 2010). Nevertheless, research addressing social functioning in NF1 is still in its infancy and the contributing factors to social problems in children with NF1 remain unclear. This thesis aimed to address gaps in the existing literature by investigating day to day social competence and social information processing in children with NF1 in greater detail.

Theoretical Framework and Clarification of Terms

The term 'social information processing' as it is used in the present thesis describes the manner in which emotional and cognitive processes interact to affect how individuals perceive and interpret social information in the environment. The term 'social competence' refers to the manner in which individuals apply this information in their social behaviours to form and maintain relationships with others. The two concepts are separate yet inextricably linked, with most theoretical models of social information processing positing that the manner in which children process and interpret social cues (e.g. facial expressions) in a given situation influences whether or not they respond in a manner which is socially competent (Crick & Dodge, 1994; Lemerise & Arsenio, 2000). For example, Crick and Dodge (1994) propose that social information processing occurs in rapid stages, beginning with attending to and encoding social cues in the situation, interpreting the information, forming goals for the situation, generating and evaluating possible responses and then enacting the most positively evaluated response. It is assumed that previous social experiences together with neurobiologically determined abilities are accessed during this processing (Lemerise & Arsenio, 2000).

Social information processing encompasses a wide range of neuropsychological processes. In this thesis, we specifically consider human faces as unique social stimuli and investigate the manner in which children with NF1 attend to, encode and interpret information from faces. We use the term 'attention to faces' to describe the manner in which visual

attention (i.e. eye gaze) is allocated towards whole or parts of faces and consider this separately from 'face perception', a term which we use to describe the ability to perceive and discriminate between the physical characteristics of faces. We distinguish this from 'face recognition' as other studies in the literature have tended to use this term to describe face recognition memory (the ability to recognise a face presented previously; e.g. Huijbregts et al., 2010). Finally, we use the term 'facial emotion recognition' to describe the ability to identify facial expressions of emotion based on characteristic combinations of facial features.

There is a paucity of literature on social information processing (and, more specifically, face processing) in children with NF1. Nevertheless, research from other developmental disorders including ASD, ADHD and 22q11.2 deletion syndrome suggests strong relationships between reduced attention to social stimuli, face perception problems and emotion recognition problems more generally (e.g. Andersson et al., 2008; Grelotti, Gauthier, & Schultz, 2002; Marsh, 2008; Wilson et al., 2010). It is interesting to note that these disorders are all characterised by difficulties forming and maintaining peer relationships (as reported in NF1) and are also associated with similar psychopathologies to NF1 (e.g. Garg, Lehtonen et al., 2013; Simon et al., 2005). As such, exploring these different aspects of face processing in children with NF1 will assist researchers and clinicians in determining whether similar social information processing abnormalities might be contributing to the behavioural phenotype in this disorder.

Aims of the Present Thesis

This thesis had three broad aims: 1) to investigate day to day social competence in children with NF1 (Paper 1), 2) to better understand facial emotion recognition skills in children with NF1 (Paper 2) and 3) to investigate face perception and attention to faces in children with NF1 (Papers 2 and 3). These broad aims were addressed across three empirical

papers, each with their own sub-aims. The papers comprise the current thesis and are outlined below.

Paper 1. Social Competence in Children with Neurofibromatosis Type 1: Relationships with Psychopathology and Cognitive Ability

Paper 1 primarily aimed to investigate social competence in school-aged children with NF1 using a comprehensive parent rating scale of social competence. Surprisingly few studies have directly investigated the day to day social competence in children with NF1. Barton and North (2004) investigated social problems and social competence in children with NF1 using the Child Behaviour Checklist (CBCL; Achenbach, 1991). On the CBCL, children with NF1 were rated by both parents and teachers as having significantly poorer social competence than their unaffected siblings, including having fewer friends and less frequent contact with friends. In keeping with these findings, Noll and colleagues (2007) found that children and adolescents with NF1 had significantly fewer reciprocal friendships and were rated as less well liked by their peers compared to their typically developing classmates, despite being rated by teachers and peers as being more prosocial in their day to day behaviour. Parents also rated children with NF1 as having significantly greater difficulties with social competence on the CBCL. No other studies to date have specifically investigated day to day social competence in children with NF1.

The reliance on the Social Problems and Social Competence indices of the CBCL as a measure of social competence in the studies by Barton and North (2004) and Noll et al. (2007) is somewhat problematic. While the CBCL is a well-standardised measure of children's skills and behaviour across a variety of domains, only four items across the Social Problems and Social Competence indices directly address the quantity and quality of children's friendships with their same-age peers (these include "gets teased", "not liked", "number of friends" and "frequency of contact with friends"), while the remainder of the

items relate more to behaviour and personality characteristics (e.g. “dependent”, “clumsy”), family relationships and participation in teams and organisations. As such, the specific nature of the day to day social competence problems reported in children with NF1 remains poorly understood.

In our study, parental ratings of day to day social competence in children with NF1 were elicited via the Social Competence with Peers Questionnaire (SCPQ–P; Spence, 1995), a nine item questionnaire with excellent psychometric properties which was specifically designed to explore interpersonal relationships, perceived popularity, and involvement in social activities in school-aged children. As this questionnaire has been normed for children aged between 8 and 17 years – and our sample included 6- and 7-year-olds – in our study we also collected SCPQ–P ratings for a sample of typically developing controls individually matched for age to our NF1 participants. Thus, using the SCPQ–P we explored parent-rated social competence in children with NF1 compared to their same-aged peers in greater detail than in previous studies.

As a sub-aim of Paper 1 we investigated whether social competence problems in children with NF1 were associated with comorbid psychopathology – in particular, ADHD or ASD symptomatology. This was important given that children with NF1 generally demonstrate strikingly high rates of ADHD and/or ASD symptomatology and given that both ADHD and ASD are associated with poor social competence in children without NF1 (Nixon, 2001; Cotugno, 2009). Conversely, it was also important to determine whether or not social competence problems would occur in children with NF1 in the absence of comorbid psychopathology. This information would assist clinicians working with children with NF1 in selecting appropriate psychological screening measures and in predicting likely areas of impairment.

Another sub-aim of Paper 1 involved investigating the association between day to day social competence and intellectual and executive functions. There is some evidence to suggest that deficits in cognitive ability contribute to social problems in NF1, with Huijbregts and De Sonneville (2011) finding that lower levels of "general cognitive ability" (a composite score composed of performances across processing speed, cognitive control and social information processing measures) were significantly associated with higher levels of emotional problems and reduced social responsiveness (that is, higher levels of autistic traits) in their sample of children and adolescents with NF1. Nevertheless, the extent to which specific cognitive deficits might contribute to day to day social competence in this population is yet to be investigated. As NF1 is known to be associated with executive dysfunction, which has been shown to be significantly related to social incompetence in the typically developing population (Razza, 2009; Riggs, Jahromi, Razza, Dillworth-Bart, & Mueller, 2006), and in other developmental disorders, including ASD (McEvoy, Rogers, & Pennington, 1993), it was important to also investigate this relationship in children with NF1. In Paper 1, we also explored the relationship between social competence and Full Scale IQ to address the possibility of a mediating effect of general intellectual ability on social competence in this group.

Paper 2. Facial Emotion Recognition, Face Scan Paths and Face Perception in Children with Neurofibromatosis Type 1

In light of evidence suggesting abnormal neural connectivity between brain regions responsible for processing social and emotional stimuli (e.g. the amygdala) in children with NF1 (Loitfelder et al., 2015), the second paper of this thesis mainly aimed to investigate facial emotion recognition skills in children with NF1. Two recent studies have revealed specific facial emotion recognition deficits in children and adults with NF1. Huijbregts et al. (2010) investigated emotion recognition skills in children and adolescents with NF1 using computerised tests from the Amsterdam Neuropsychological Tasks battery (De Sonneville,

1999), and found that, on a forced choice matching task, children with NF1 displayed significantly poorer recognition accuracy for fearful facial expressions compared to controls, but not happy, sad or angry expressions. The authors also reported that children with NF1 were significantly less accurate than neurotypical controls in identifying pairs of fearful and angry facial expressions on an additional task requiring participants to indicate whether two pictures presented simultaneously on a screen displayed the same emotion. In a more recent study, Pride and colleagues (2014) examined emotion recognition skills in adults with NF1 using The Awareness of Social Inference Test (TASIT; McDonald, Flanagan, Rollins, & Kinch, 2003). For the emotion recognition portion of the TASIT, participants were required to watch brief video vignettes of an actor and were asked to identify the emotion portrayed (neutral, happy, sad, angry, disgusted, fearful, or surprised) in a forced choice recognition format. On this task, adults with NF1 displayed an isolated problem in recognising anger compared to healthy controls. Taken together, these findings suggest impairments in the ability to recognise negative or threatening emotions (when presented as both static and dynamic stimuli) in people with NF1.

Pride et al. (2014) speculated that facial emotion recognition deficits in NF1 might reflect aberrant visual scanning of facial features (e.g. less time visually scanning core features such as the eyes or mouth) or, alternatively, more general deficits in face perception (the ability to perceive and discriminate between faces). However, no study to date has directly explored these possibilities. In Paper 2, using a combination of behavioural measures and eye-tracking technology, we investigated the relationships between face scan paths, face perception, and emotion recognition skills in children with NF1.

The primary aim of Paper 2 was to further investigate emotion recognition abilities for threatening (negative) versus non-threatening faces in children with NF1 by using a forced choice recognition paradigm with face stimuli selected from the Ekman standardised face set

(Ekman & Friesen, 2003) displaying neutral, happy, angry and fearful expressions. We further extended the existing literature by exploring variables which may underlie facial emotion recognition problems in children with NF1. Specifically, we used eye tracking technology to record participants' scan paths towards the emotion recognition stimuli during a passive viewing paradigm and directly investigated whether children with NF1 spent less time viewing core facial features (and in particular, the eye region) compared to typically developing controls individually matched for age. We also investigated whether children with NF1 displayed deficits in face perception on the Facial Recognition Test (Benton, Sivan, Hamsher, Varney, & Spreen, 1994) compared to controls. As we chose not to exclude children with comorbid ADHD from our NF1 sample, and because ADHD has been associated with face processing abnormalities in the absence of NF1 (Marsh, 2008), we also investigated the relationships between comorbid ADHD symptomatology and our variables of interest in the NF1 group. As detailed above, the relationships between emotion recognition skills and these variables were investigated using correlational analyses.

Paper 3. How Children with Neurofibromatosis Type 1 Process Faces within a Social Scene

In Paper 3 we utilised eye-tracking technology to compare the manner in which individuals with NF1 and controls attended to faces presented in the context of a social scene. Specifically, we investigated whether children with NF1: i) took longer to first fixate on face stimuli within a scene and ii) spent less time overall viewing faces within a social scene compared to age-matched, typically developing controls. These are important research questions to consider in children with NF1 in light of emerging evidence suggesting deficits in visuoperception, general attention skills and social information processing in this population (e.g. Huijbregts et al., 2010; Huijbregts & De Sonneville, 2011; Hyman et al., 2005; Payne et al., 2011).

Literature on the development of face recognition skills suggests an integral relationship between attention to faces in the natural environment and the development of face perception abilities. The leading theory suggests that, via a specific subcortical mechanism, infants display an innate attentional bias towards faces in their environment (Morton & Johnson, 1991). As such, infants will be exposed to a large number of human faces throughout their development and it is argued that, via this process, brain tissue in the inferotemporal cortex becomes specialised for face perception. In keeping with this theory, impaired face perception and reduced attention to faces have been shown to be related in individuals with ASD (e.g. Grelotti et al., 2002; Wilson, Brock, & Palermo, 2010). Nevertheless, no studies to date have investigated the relationship between face perception and attention to faces in children with NF1. In our study, we investigated this relationship in both our NF1 and control groups using correlational analyses.

Summary

In summary, this thesis investigated socio-emotional functioning in children with NF1 compared to their typically developing peers. There were three primary aims: 1) to investigate day to day social competence, 2) to better understand facial emotion recognition abilities and 3) to explore face processing and attention to faces in children with NF1. This thesis introduced novel investigations regarding the social-cognitive phenotype in children with NF1, particularly pertaining to the manner in which they perceive and attend to information from faces. These investigations have important implications for the clinical management of children with this condition.

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PAPER 1

Social Competence in Children with Neurofibromatosis Type 1: Relationships with Psychopathology and Cognitive Ability

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Abstract

This study investigated parent ratings of day to day social competence in 23 children with neurofibromatosis type 1 (NF1) aged between 6 and 13 years compared to 23 chronological age-matched typically developing controls using a brief, standardised questionnaire – the Social Competence with Peers Questionnaire (Spence, 1995). The relationships between social competence, psychopathology (parent ratings of Attention Deficit Hyperactivity Disorder or Autism Spectrum Disorder symptomatology), and cognitive ability (Full Scale IQ and parent ratings of functional executive behaviour) in children with NF1 were also explored. Results indicated that children with NF1 displayed significantly poorer day to day social competence than controls. These social competence deficits were not related to Attention Deficit Hyperactivity Disorder symptomatology, Full Scale IQ or functional executive behaviour. However, social competence problems were significantly related to Autism Spectrum Disorder symptomatology and socially anxious/avoidant behaviours as assessed by Social Motivation scores on the Social Responsiveness Scale (Constantino, 2002) in our NF1 cohort. These results suggest a need to incorporate screening for social competence problems and comorbid psychopathology into the more general clinical management of children with NF1.

Key Words: NF1, social competence, psychopathology, cognitive ability.

Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder with an estimated prevalence of approximately 1 in 3,000. The condition is caused by a mutation of the NF1 gene on the long arm of chromosome 17 (Yohay, 2006) and is associated with distinctive physical characteristics, neurofibromas (benign tumours); skinfold freckling; café-au-lait macules (pigmented birthmarks) and Lisch nodules (melanocytic hamartomas affecting the iris) (Williams et al., 2009). There is considerable variability in the clinical presentation of children with NF1 (Szudek, Birch, Riccardi, Evans, & Friedman, 2000), however common complications of the condition include specific cognitive impairments (Hyman, Shores, & North, 2005; Huijbregts & De Sonneville, 2011) and a high prevalence of psychological comorbidities (Garg, Lehtonen, et al., 2013; Johnson, Saal, Lovell, & Schorry, 1999). Poor social skills and difficulties with interpersonal relationships have also been reported in NF1 (Barton & North, 2004; Noll et al., 2007), although the latter is particularly under-researched. As such, the aim of the current study was to investigate, in greater detail, the nature of day to day social competence difficulties in children with NF1. A second and related aim was to investigate how levels of social competence in children with NF1 might relate to cognitive dysfunction and/or symptoms of psychopathology.

Specific Cognitive Impairments

Cognitive impairment is widespread in NF1, affecting approximately 80% of children with the condition (Hyman et al., 2005). Deficits in attention, visuospatial skills, language, and executive function (including planning, organisation, inhibition, and self-monitoring) are most common (e.g. Hyman et al., 2005; Lehtonen, Howie, Tump, & Huson, 2013; Payne, Hyman, Shores, & North, 2011; Rowbotham, Pit-ten Cate, Sonuga-Barke, & Huijbregts, 2009). In contrast, intellectual functioning typically falls broadly within the normal range, although a distinct and reliable downward shift in overall intelligence levels compared with

both the general population and unaffected sibling controls has been consistently reported (Feldmann, Denecke, Grenzebach, Schuierer, & Weglage, 2003; Ferner, Hughes, & Weinman, 1996; Hyman et al., 2005). Academic difficulties are also common, with between 50 and 70% of children with NF1 demonstrating impairments in literacy or numeracy skills (Brewer, Moore, & Hiscock, 1997; Hyman, Shores, & North, 2006) and approximately 20% estimated to meet criteria for a learning disability (Hyman et al., 2006).

Psychological Comorbidities

Recent studies have documented a wide range of psychological disorders associated with NF1 (e.g. Garg, Lehtonen, et al., 2013; Pasini et al., 2012). Reports indicate that Attention Deficit Hyperactivity Disorder (ADHD) occurs in 30% to 50% of individuals with NF1 (Hofman, Harris, Bryan, & Denckla, 1994; Hyman et al., 2005; Mautner, Kluwe, Thakker, & Leark, 2002). This is high compared to the rate of approximately 5% in the general population (American Psychiatric Association, 2013). Children with NF1 also display a significantly higher prevalence of autism spectrum disorder (ASD) symptomatology compared to the general population, with three recent studies reporting that between 11% and 29% of children with NF1 are rated within the severe range on a screening measure of ASD symptomatology; a range which is strongly associated with a clinical diagnosis of ASD (Adviento et al., 2014; Garg, Lehtonen, et al., 2013; Walsh et al., 2013). Importantly, however, NF1 is associated with impairments in several domains that overlap with ASD (including delayed social, executive, and language skills), and so the true prevalence of ASD in NF1 may be lower than these reports would indicate (Payne, 2013). Nevertheless, a recent population-based epidemiologic study of children and adolescents in with NF1 using diagnostic assessment tools estimated a population ASD prevalence of 24.9% (Garg, Green, et al., 2013), well above the estimated general population prevalence of 1.5% (Baio, 2012).

In addition to ADHD and ASD, there is some evidence to suggest a predisposition towards anxiety disorders in children with NF1 (Pasini et al., 2012). The prevalence of anxiety disorders in the adult NF1 population has been estimated at between 1% and 6% (Belzeaux & Lancon, 2006), which is generally in keeping with the rates observed in the general population (Kessler et al., 2009). Nevertheless, Pasini et al. (2012) showed that children and adolescents with NF1 display significantly higher levels of anxiety symptomatology on a self-report measure compared to healthy controls, although these children did not differ significantly from controls on any disorder-specific subscales, including: physical symptoms; harm avoidance; social anxiety and separation panic. The authors noted a moderate correlation between social anxiety symptoms and disease severity, such that participants with more severe physical manifestations of NF1 reported significantly higher levels of social anxiety (Pasini et al., 2012). Notably, however, significant anxiety (and particularly social anxiety) has been documented in ADHD (Bowen, Chavira, Bailey, Stein, & Stein, 2008; Schatz & Rostain, 2006) and ASD (Bellini, 2004; Bellini, 2006), making it difficult to tease apart these psychological comorbidities in children with NF1.

Social Skills in NF1

Research addressing social functioning in NF1 is in its infancy and has tended to focus primarily on social information processing (especially emotion recognition skills), emotional problems, and social behaviour (e.g. Huijbregts, Jahja, De Sonneville, De Breij, & Swaab-Barneveld, 2010; Pride, Crawford, Payne, & North, 2013). For example, Huijbregts and De Sonneville (2011) found that children with NF1 display significantly higher levels of emotional, conduct and peer-related problems compared to typically developing controls. Their NF1 cohort also performed significantly worse than controls on social information processing tasks that required them to identify and match facial expressions of emotion. In keeping with these findings, specific emotion recognition deficits have been documented in

children with NF1, with Huijbregts et al. (2010) showing that children and adolescents with NF1 demonstrate significant difficulty recognising and matching facial expressions of fear and anger. The same emotion recognition deficits have also been documented in the adult NF1 population, with additional deficits evident in identifying whether conversational exchanges were sincere or sarcastic (Pride et al., 2014).

In general, informant reports of social and emotional functioning in children with NF1 indicate a high incidence of social and behavioural problems (Barton & North, 2004; Descheemaeker et al., 2005; Dilts et al., 1996; Huijbregts & De Sonneville, 2011). Furthermore, several studies have documented discrepancies between self-report ratings of social skills and informant (parent and teacher) ratings, suggesting that children with NF1 may perhaps lack awareness of their own social and behavioural difficulties (Barton & North, 2004; Descheemaeker et al., 2005). Similar patterns have been documented in adults with NF1, who have been reported to display less prosocial behaviour than the normal population, as well as reduced awareness of their deficits in social skills (Pride et al., 2013). Taken together, these findings suggest deficits in aspects of social awareness, social perception and social cognition in this population.

Social Competence in NF1

Anecdotally, children with NF1 demonstrate considerable social difficulties on a day to day level, with reports from children with NF1 and their parents suggesting that they are often teased and rejected by their peers and have difficulty forming and maintaining friendships (Benjamin et al., 1993). Nevertheless, only two studies to date have directly examined social competence in children in NF1. Barton and North (2004) investigated social skills and social outcomes in children with NF1 using parent and teacher ratings on the Social Skills Rating System (SSRS; Gresham & Elliott, 1990) and the Child Behaviour Checklist (CBCL; Achenbach, 1991). Children with NF1 were rated by both parents and teachers as

having significantly poorer social competence compared with their unaffected siblings, despite there being no significant difference between the groups in terms of their general social skills, including: cooperativeness; assertiveness; responsibility and self-control. The presence of ADHD was found to significantly increase the risk of social competence problems in children with NF1, with those with a comorbid ADHD diagnosis[1] performing significantly worse on measures of social competence; they also displayed significantly greater difficulty with social skills and social problems. In keeping with these findings, Noll and colleagues (2007) found that children and adolescents with NF1 had significantly fewer reciprocal friendships and were rated as less well liked by their peers compared to their typically developing classmates, despite being rated by teachers and peers as being more prosocial. Parents also rated children with NF1 as having significantly greater difficulties with social competence on the CBCL. The authors noted that social difficulties in their sample appeared to be the most severe for those children with comorbid learning difficulties and/or ADHD; however, this was not formally addressed statistically (Noll et al., 2007).

There is some evidence to suggest that general cognitive ability may be related to social and behavioural functioning in NF1, although the exact nature of the relationship between social competence and cognitive ability in this population remains unclear. Huijbregts and De Sonneville (2011) reported that deficits in general cognitive ability (a composite score comprising measures of processing speed, social information processing, and cognitive control) contributed significantly to emotional problems and reduced social responsiveness in children and adolescents with NF1. Nevertheless, the impact of specific cognitive impairments on day to day social competence (for example, the role of executive dysfunction) requires further investigation. Notably, NF1 is associated with significant functional executive difficulties, with particular deficits evident in sustaining working

[1] ADHD was diagnosed in this study based on parent and teacher questionnaire ratings, neuropsychological test performance, and clinical presentation as part of a concurrent study (Barton & North, 2004).

memory, self-monitoring, and planning and organisation (Payne et al., 2011). Executive function and social competence have been shown to be significantly related in the typically developing population (Razza, 2009; Riggs, Jahromi, Razza, Dillworth-Bart, & Mueller, 2006), and in other developmental disorders, including ASD (McEvoy, Rogers, & Pennington, 1993), but no published study to date has directly investigated the relationship between executive function and social competence in NF1.

Previous research on social competence in children with NF1 has relied heavily on the Social Problems and Social Competence indices of the CBCL (e.g. Barton & North, 2004; Dilts et al., 1996; Noll et al., 2007). While this is a valid, reliable, standardised and commercially available measure, only four items across both of these indices directly address the quantity and quality of children's friendships with their same-age peers[2], with the remainder of the items relating to behaviour and personality characteristics (e.g. "dependent", "clumsy"), as well as family relationships and participation in teams and organisations. As such, the precise nature of the social competence problems reported in children and adolescents with NF1 remains unclear and warrants further investigation. Furthermore, no published studies to date have directly explored whether interpersonal relationships in NF1 are associated with cognitive and/or psychological impairment. It is extremely important to identify the nature of social competence problems in children with NF1 and potential cognitive and psychological risk factors, as this information will assist clinicians working with these children in selecting appropriate screening measures and providing targeted intervention recommendations.

[2] The Social Problems index on the CBCL contains only two out of 11 items ("gets teased" and "not liked") which directly pertains to the quality of children's relationships with their peers. Similarly, the CBCL Social Competence index contains only two items relating to children's friendships ("number of friends" and "frequency of contact with friends").

Aims of the Current Study

In light of the above, the primary aim of the present study was to gain a more comprehensive understanding of day to day social competence in children with NF1 using the parent form of the Social Competence with Peers Questionnaire (SCPQ–P; Spence, 1995), a nine item questionnaire with excellent psychometric properties which was specifically designed to explore interpersonal relationships, perceived popularity, and involvement in social activities in school-aged children. In keeping with previous findings (e.g. Barton & North, 2004; Noll et al., 2007), it was hypothesised that, overall, children with NF1 would demonstrate poorer social competence compared with their typically developing peers (Hypothesis 1). However, given the variability observed in the clinical phenotype of children with NF1 (e.g. Levine, Materek, Abel, O'Donnell, & Cutting, 2006; Szudek et al., 2000), significant variability in their social competence was also anticipated (Hypothesis 2).

The second aim of this study was to examine the relationships between social competence and ADHD and ASD symptomatology in children with NF1. Although previous studies have indicated poorer social skills and social competence in children with NF1 and comorbid ADHD (e.g. Barton & North, 2004; Noll et al., 2007), the potential influence of autistic traits on social outcomes in NF1 has received little empirical attention. As up to one quarter of children with NF1 demonstrate significantly elevated symptoms of both ADHD and ASD (Garg, Lehtonen, et al, 2013), it is important to determine to what extent ADHD and ASD symptomatology are contributing to social competence problems in NF1. Conversely, it is also important to determine whether or not social competence difficulties exist in NF1 in the absence of comorbid psychopathology. It was hypothesised that reduced social competence would be identified even in children with NF1 and no psychological diagnosis (Hypothesis 3). It was also hypothesised that higher levels of both ADHD and ASD

symptomatology would be related to poorer social competence in children with NF1 (Hypothesis 4).

The final aim of the present study was to investigate the relationship between social competence and cognitive functioning in children with NF1, particularly general intellectual functioning (FSIQ) and executive function. It was hypothesised that social competence would not be related to overall levels of intellectual functioning in children with NF1 (Hypothesis 5). In keeping with observations from typically developing children (Razza, 2009; Riggs et al., 2006), it was hypothesised that social competence would be related to day to day executive function in children with NF1, such that children with more executive difficulties would display lower social competence (Hypothesis 6).

Method

Participants

NF1 participants in this study were recruited through the Neurogenetics Clinic at The Children's Hospital at Westmead (CHW), Sydney, Australia. This clinic has a wide referral base and caters for over 1300 individuals with NF1, with all socioeconomic groups represented. Questionnaires were provided to the parents of 30 children with NF1 who were participating in additional research studies at CHW from January 2011 to February 2014. These children met the following inclusion criteria: (a) confirmed diagnosis of NF1 based on criteria specified by the National Institutes of Health Consensus Conference (NIH, 1988); (b) absence of diagnosed intracranial pathology (e.g. epilepsy, traumatic brain injury, or brain tumour); (c) an IQ $\geq$ 70; (d) no current or previous diagnosis of anxiety disorder, mood disorder, or psychotic disorder identified from review of clinical records; and (e) competency in the English language. No NF1 participants had to be excluded based on these criteria. Of the 30 sets of questionnaires provided, seven were not returned, leaving a final sample of 23 children with NF1 (15 females, 8 males) aged between 6.67 and 13.83 years (M = 10.04, SD =

2.12). The 'no response' group (6 females, 1 male) had a mean age of 10.82 years (*SD* = 1.55) and a mean FSIQ of 90.43 (*SD* = 12.93), and did not differ significantly from the participants included in the present study on any demographic variables (all, $p > .10$). A review of clinical records revealed that five NF1 participants had a diagnosis of ADHD. No NF1 participant had a diagnosis of ASD. For NF1 participants, Full Scale IQ (FSIQ) was established using the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2003).

Twenty-three typically developing (TD) controls (9 females, 14 males) were recruited through Neuronauts: a kids' science club at Macquarie University, Sydney, Australia. TD participants were aged between 6.67 and 13.42 years (*M* = 9.92, *SD* = 1.97). TD control children were excluded from the study if they had a history of developmental delay, IQ < 70, sensory impairments, diagnosed neurological or psychiatric disorder, or English as a second language. No TD controls had to be excluded based on these criteria. As a screening measure, FSIQ was estimated for TD control participants using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999).

NF1 and TD control groups were matched for chronological age (within 6 months of age) at the individual level and handedness at the group level. Table 1 displays the demographic characteristics of each group. As shown in Table 1, a chi-square test revealed no significant difference in sex distribution between the groups, although a non-significant trend was observed. Independent samples *t* test revealed the two groups were well matched in terms of age. Consistent with literature showing downward shifts in FSIQ in NF1 (Feldmann et al., 2003; Ferner et al., 1996; Hyman et al., 2005), the two groups differed significantly in terms of their FSIQ scores, albeit on different measurement instruments. On average, the NF1 group fell within the low average IQ range and the TD control group fell within the average IQ

range. Overall, the clinical sample was considered to be adequately representative of the wider NF1 population and the TD group were considered to be typically developing.[3]

Table 1

Demographic characteristics for each group.

	NF1 group *Mean (SD)* *Range*	TD group *Mean (SD)* *Range*	*t* score	*p* value
Males : Females	8 : 15	14 : 9	3.136*	.077
Chronological Age	10.04 (2.12) 6.67 – 13.83	9.92 (1.97) 6.67 – 13.42	0.210	.835
FSIQ	87.48 (10.33)[a] 71.00 – 109.00	107.61 (12.40)[b] 79.00 – 134.00	-5.981	< .001

Note: Chronological age is in years. FSIQ scores from both the WISC-IV and WASI are standardised against a normative mean of 100.00 and a standard deviation of 15.00.
* Chi-square statistic
[a] FSIQ measured using WISC-IV
[b] FSIQ measured using WASI

Materials

Both Groups:

Social Competence With Peers Questionnaire – Parent Form (SCPQ–P)

Social competence was assessed using the SCPQ–P (Spence, 1995), a nine item questionnaire addressing the quality and quantity of children's friendships, perceived popularity, the nature of their relationships with children of the same age, and their involvement in social activities (e.g. being invited to parties and seeing friends at weekends). Items are rated on a three-point Likert scale from 0 (not true) to 2 (mostly true), with higher scores indicating greater social competence. The psychometric properties of this scale are very respectable, with a reported Guttman split-half reliability coefficient of 0.87 and coefficient alpha of 0.81 (Spence, 1995). The SCPQ–P was developed to elicit parental assessment of social competence difficulties in school-aged children, with the goal of

[3] One TD control participant fell at the upper end of the borderline IQ range, and two TD participants had IQs > 120, however these participants were not outliers from the TD group as a whole in terms of their SCPQ–P ratings. Notably, FSIQ did not correlate significantly with SCPQ–P ratings in the TD control sample (p = .369).

providing details for targeted intervention for children with social problems. As such, it is well-suited to the investigation of social competence in a clinical population.

There are normative data for the SCPQ–P for children aged between 8 and 17 years (Spence, 1995). In this sample, the mean parent rating was 14.82/18 (SD = 3.12), and there was no effect of age or gender. However, as the sample in the present study included 6 and 7 year olds, it was considered most appropriate to compare results against a sample individually matched for chronological age.

NF1 Group:

Conners 3 – Parent Long Form (Conners 3–PL)

The Conners 3–PL (Conners, 2008) was administered to the NF1 group. The Conners 3–PL is a standardised, commercially available measure used to assist in the evaluation, diagnosis and treatment response of children with ADHD. It provides standardised scores of ADHD symptoms, as well as comorbid disorders including Oppositional Defiant Disorder and Conduct Disorder. The scale comprises 105 items, each rated on a four-point Likert scale from 0 (not at all true) to 3 (very much true), with higher scores indicating greater difficulty. These items contribute to six separate content scales: Inattention, Hyperactivity/Impulsivity, Learning Problems, Executive Functioning, Defiance/Aggression, and Peer Relations. Raw scores are converted into T-scores based on age and gender norms. T-scores between 60 and 64 are considered "elevated" and are associated with more concerns than is normal, while T-scores ≥ 65 on each scale are "very elevated" and indicate significant areas of concern.

Social Responsiveness Scale (SRS) Parent Form

The parent form of the SRS (Constantino, 2002) was administered to the NF1 group. The SRS is an instrument designed to identify social difficulties and symptoms of autism spectrum disorders in children and adolescents aged between 4 and 18 years. The SRS comprises 65 items that form five separate treatment subscales: Social Awareness, Social

Cognition, Social Communication, Social Motivation (including socially anxious and avoidant behaviours), and Autistic Mannerisms.[4] Items are rated on a four-point Likert scale from 1 (never true) to 4 (almost always true) and raw scores are converted into T-scores based on gender norms, with higher scores indicating greater social difficulties. Scores obtained across the treatment subscales are summed to provide a SRS total score. Total SRS T-scores between 60 and 75 (mild to moderate range) indicate clinically significant levels of autistic traits and are typical for children with less severe ASD (Constantino, 2002). Total SRS T-scores of 76 or more (severe range) indicate a severe interference in everyday social interactions and are strongly associated with the presence of ASD. At the treatment subscale level, T-scores ≥ 60 are considered clinically significant and suggest that a particular area may require treatment or intervention (Constantino, 2002). The SRS has respectable psychometric properties and has previously been used to investigate autism spectrum symptomatology in populations with NF1 (Adviento et al., 2014; Garg, Lehtonen, et al., 2013; Walsh et al., 2013).

Behavior Rating Inventory of Executive Function (BRIEF) - Parent Version

Parents/guardians of the NF1 group completed the BRIEF (Gioia, Isquith, Guy, & Kenworthy, 2000). The BRIEF comprises 86 items aimed at assessing day to day executive abilities. These items contribute to eight separate subscales: Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor. Scores on the Inhibition, Shift, and Emotional Control subscales are summed to provide a Behavioral Regulation Index, and scores on the remaining subscales are summed to provide a Metacognition Index. A global composite score (Global Executive Composite) is also generated, incorporating all eight subscales. Raw scores on all indices are converted into T-scores based on age norms, with higher T-scores indicating more problematic behaviours. T-

[4] Complete descriptions of all SRS treatment subscales are provided in Appendix.

scores ≥ 65 are considered clinically significant. The BRIEF has high internal consistency (0.80 to 0.98) and high test-retest reliability (Gioia, Isquith, Retzlaff, & Espy, 2002).*Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV)*

The WISC-IV (Wechsler, 2003) is one of the most widely used measures of intelligence for children aged between 6 and 16 years. The WISC-IV is made up of ten core subtests which contribute to four composite indices (Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed), as well as a global FSIQ score. The test takes between 60 and 80 minutes to administer. There are published WISC-IV Australian norms, with scores standardised against a mean of 100 and a standard deviation of 15.

Results

Data were analysed using Predictive Analytics SoftWare (PASW) Version 18 for Windows. Initial investigations revealed that data were not normally distributed and that there was unequal variance between groups, so non-parametric analyses were used. Mean raw scores on the SCPQ–P and standardised T-scores on the SRS, Conners 3–PL, and BRIEF subscales were compared between groups using the Mann-Whitney U test. Relationships between social competence, Conners 3–PL ratings, SRS ratings, BRIEF ratings, and FSIQ in the NF1 group were examined using Spearman's rho correlations. Correlations were based on SCPQ–P raw scores and standardised (age-adjusted) scores for all other measures. This was considered to be appropriate, as a previous normative study revealed that there was no effect of age on SCPQ–P ratings in a typically developing sample aged between 8 and 17 years (Spence, 1995). Furthermore, statistical investigations revealed that there was no relationship between age and SCPQ–P raw scores in the present NF1 sample (ρ = -.16, p = .463).

Due to the relatively small sample size in the present study, a p value of .05 was used for all analyses to indicate statistical significance in order to reduce the likelihood of Type II error (Rothman, 1990).

Do children with NF1 display lower and more variable social competencies than their TD peers?

Figure 1 shows the mean social competence ratings for NF1 and TD control groups. On the SCPQ–P, the NF1 group displayed significantly lower overall social competence ratings compared to TD controls (Z = -2.59, p = .010)[5]. Moreover, Levene's test for equality of variances revealed significantly greater variability in total social competence ratings for the NF1 children compared with the TD control group (F = 20.73, p < .001). The distribution of SCPQ–P scores for participants in both groups is displayed in Figure 2.

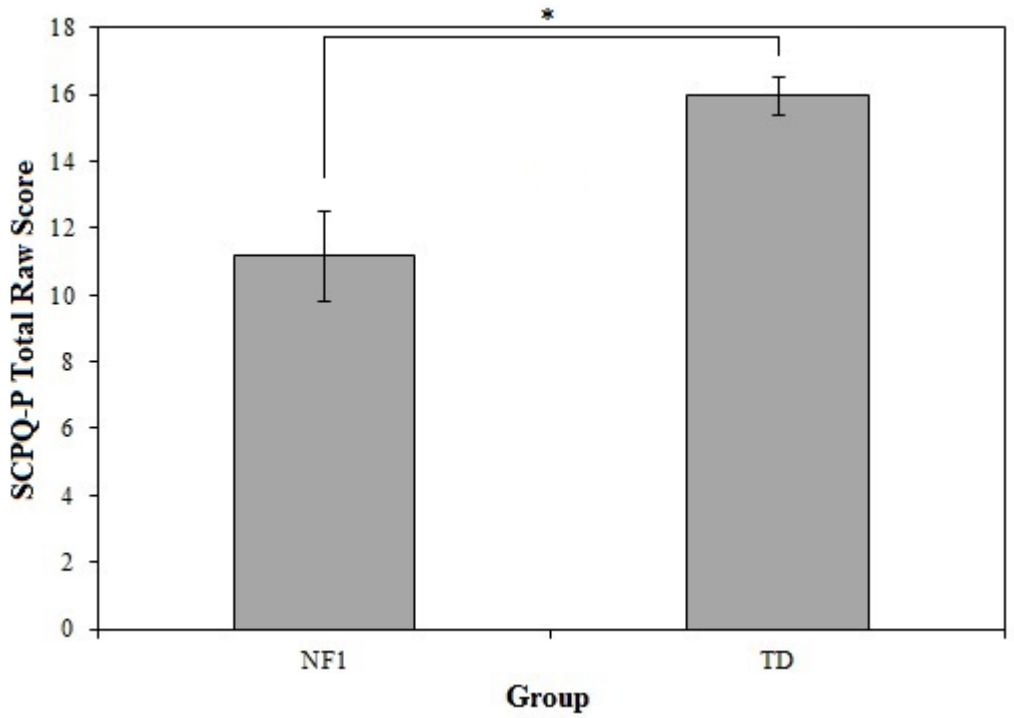

Figure 1. Mean SCPQ–P ratings for NF1 and TD control groups. Bars represent +/- 1 standard error. * = p < .05.

Item-level analyses revealed that NF1 children displayed significantly lower ratings on the following items compared to controls: 'has at least one close friend' (Z = -3.29, p = .001), 'has stable friendships with other kids his/her age' (Z = -2.77, p = .006), 'finds it easy to make friends' (Z = -2.31, p = .021), 'has good relationships with classmates' (Z = -2.34, p = .020),

[5] The mean for the NF1 sample was also compared with the normative mean (Spence, 1995) using the One-Sample Wilcoxon Signed Ranks Test. The NF1 group displayed significantly lower social competence ratings than the normative population (p = .033).

'is popular amongst others his/her age' (Z = -3.16, p = .002), and 'sees a friend or friends socially at weekends' (Z = -2.62, p = .009). Ratings were similar between NF1 and TD groups on the following items: 'other kids invite him/her to their homes' (Z = -1.88, p = .060), 'other kids invite him/her to social events or activities' (Z = -1.89, p = .059), and 'gets invited to parties' (Z = -1.69, p = .090).

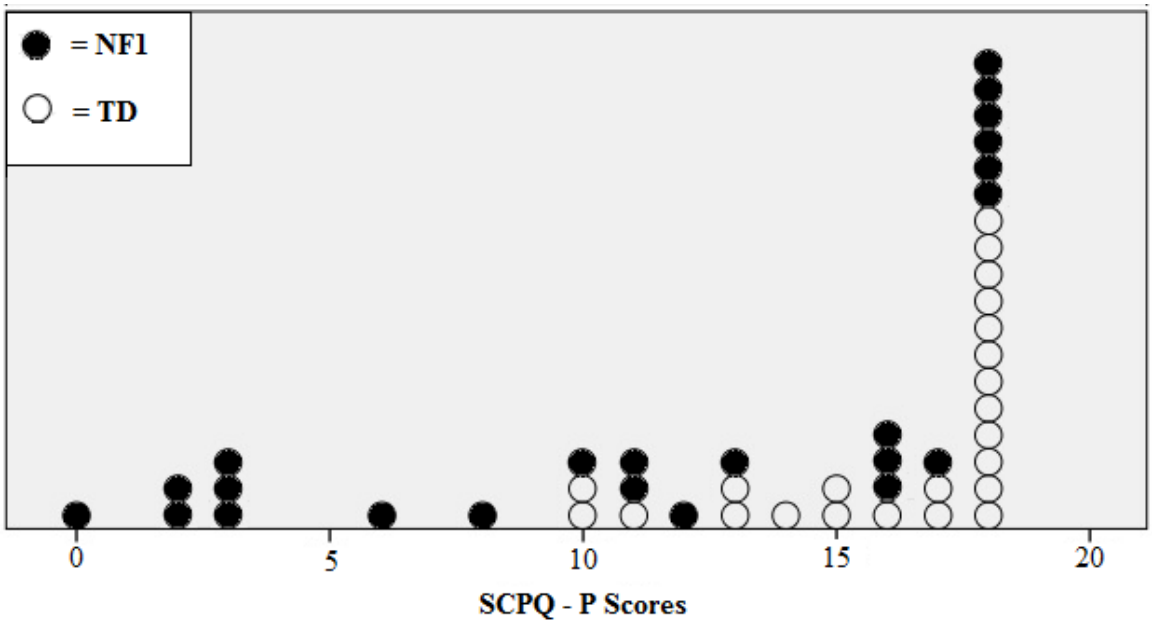

Figure 2. Dot plot showing distribution of social competence ratings for NF1 and TD control participants.

To address the possibility of bias due to gender effects on SCPQ–P ratings, correlations between these variables were examined for the NF1 and TD control groups. There was no significant effect of gender on SCPQ–P ratings (both, $p \geq .236$)[6].

Do those children with NF1 who do not have co-morbid ADHD or ASD demonstrate social competence difficulties?

To determine whether NF1 participants with no comorbid ADHD or ASD diagnosis demonstrate social competence difficulties, the previous analyses were repeated after exclusion of the five NF1 participants with a comorbid psychological diagnosis (ADHD).

[6] The effect of age on social competence in both groups was also explored using Spearman's rho correlations. There was a significant positive correlation between age and social competence in the TD group (ρ = .52, p = .012) but not in the NF1 group (ρ = -.16, p = .463).

Even after exclusion of those participants with psychological comorbidities, the NF1 group displayed significantly lower overall social competence ratings compared to TD controls (Z = -2.01, p = .045). Again, Levene's test for equality of variances revealed significantly greater variability in total social competence ratings for the NF1 children compared with the TD control group (F = 9.65, p = .004).

General Performance on Psychological and Cognitive Questionnaire Measures

Conners 3–PL ratings in the NF1 group

Table 2 shows the mean Conners 3–PL ratings for the NF1 group and the percentage of the sample falling within the "very elevated" or clinical range (mean T-scores ≥ 65) on each subscale. On average, the NF1 group displayed very elevated ratings on the domains of Inattention and Learning Problems relative to the normative population. However, parent ratings of Hyperactivity/Impulsivity, Executive Functioning, Defiance/Aggression, and Peer Relations were within normal limits (mean T-scores < 65).

Table 2

Mean T-scores on the Conners 3–PL for the NF1 group.

	Mean (SD) *Range*	*% in Very Elevated Range*
Inattention	66.61* (14.30) 45.00 – 90.00	43.48% (n = 10)
Hyperactivity/Impulsivity	62.52 (16.49) 42.00 – 90.00	39.13% (n = 9)
Learning Problems	69.91* (12.85) 49.00 – 90.00	56.52% (n = 13)
Executive Functioning	61.09 (12.50) 38.00 – 86.00	39.13% (n = 9)
Defiance/Aggression	54.70 (13.73) 41.00 – 90.00	21.74% (n = 5)
Peer Relations	62.70 (16.41) 43.00 – 90.00	39.13% (n = 9)

Note: T-scores have a mean of 50 and a standard deviation of 10. Scores ≥ 65 on the Conners 3–PL represent areas of clinical significance.
* T-score ≥ 65

The distribution of ADHD symptoms of Inattention and Hyperactivity/Impulsivity in the NF1 group are displayed in dot plots for reference (Figures 3 and 4).

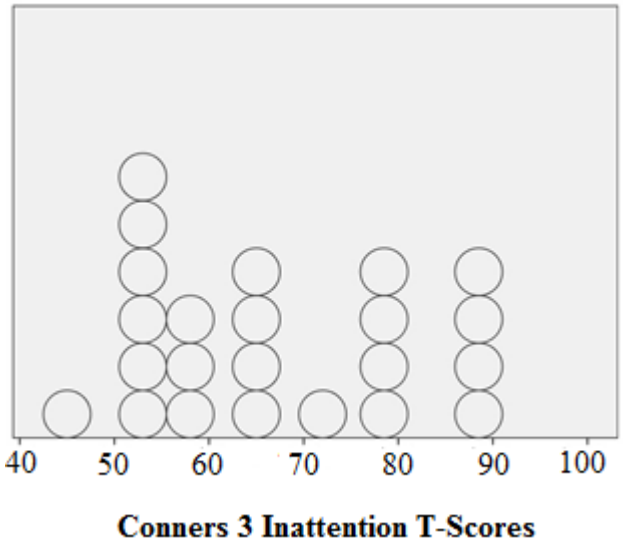

Figure 3. Dot plot showing distribution of Conners 3 Inattention T-scores in the NF1 group.

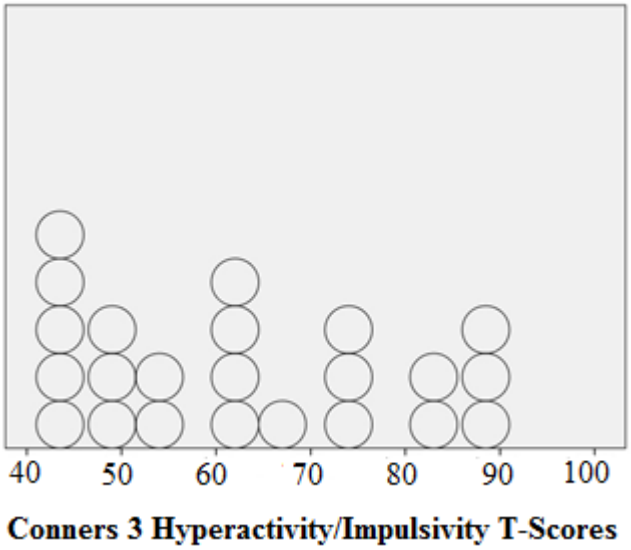

Figure 4. Dot plot showing distribution of Conners 3 Hyperactivity/Impulsivity T-scores in the NF1 group.

Social Responsiveness Scale ratings in the NF1 group

Table 3 shows the average SRS profiles for the NF1 group. Notably, 17.39% (n = 4) of the NF1 group fell within the severe range (total T-score > 75), a range which is typically associated with a clinical diagnosis of ASD (see Figure 5 for distribution of scores). The most

commonly reported difficulties in the NF1 group were related to Social Motivation (socially anxious and avoidant behaviours), which were clinically elevated in 43.48% (n = 10) of the NF1 sample. This was followed by Autistic Mannerisms (e.g. unusually narrow range of interests, repetitive behaviours), which were clinically elevated in 39.13% (n = 9) of the NF1 group.

Table 3

Mean T-scores on the Social Responsiveness Scale (SRS) for the NF1 group.

	Mean (SD) *Range*	*% in Clinical Range* *Mild to Moderate* *(60 ≤ T < 76)*	 *Severe* *(T > 75)*
Social Awareness	55.52 (13.72) 38.00 – 91.00	26.09% (n = 6)	4.35% (n = 1)
Social Cognition	57.61 (15.87) 36.00 – 92.00	21.74% (n = 5)	17.39% (n = 4)
Social Communication	58.65 (13.99) 42.00 – 88.00	21.74% (n = 5)	17.39% (n = 4)
Social Motivation	57.52 (12.58) 40.00 – 89.00	34.78% (n = 8)	8.70% (n = 2)
Autistic Mannerisms	63.39* (18.24) 40.00 – 105.00	13.04% (n = 3)	26.09% (n = 6)
SRS Total Score	60.09 (15.49) 41.00 – 93.00	26.09% (n = 6)	17.39% (n = 4)

Note: T-scores have a mean of 50 and a standard deviation of 10. T-scores ≥ 60 are considered clinically elevated.
* T-score ≥ 60

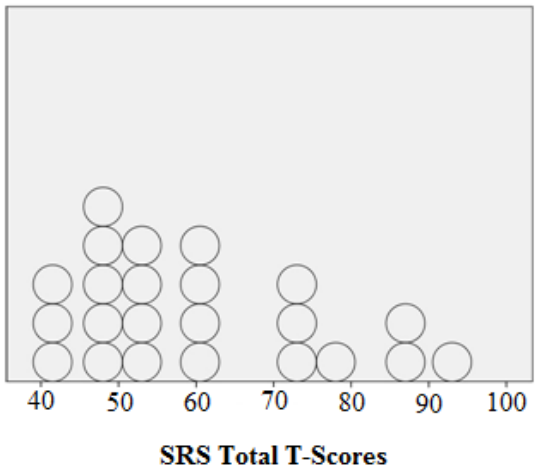

Figure 5. Dot plot showing distribution of Social Responsiveness Scale Total T-scores in the NF1 group.

BRIEF ratings in the NF1 group

Table 4 shows the average BRIEF ratings for the NF1 group. On average, the NF1 group fell within normal limits on all BRIEF indices (all mean T-scores < 65). The most commonly reported domain of difficulty was Working Memory (occurring in almost 40% of the cohort), followed by Initiate, Shift and Plan/Organize.

Table 4

Mean T-Scores on the Behavior Rating Inventory of Executive Function in the NF1 Group

	Mean (SD) *Range*	*% in Clinically Significant Range*
Inhibit	52.83 (12.58) 38.00 – 87.00	17.39% (n = 4)
Shift	55.74 (14.79) 39.00 – 88.00	30.43% (n = 7)
Emotional Control	52.52 (14.15) 36.00 – 80.00	17.39% (n = 4)
Behavior Regulation Index	53.91 (13.80) 36.00 – 86.00	21.74% (n = 5)
Initiate	58.39 (12.26) 40.00 – 79.00	34.78% (n = 8)
Working Memory	60.26 (11.09) 36.00 – 81.00	39.13% (n = 9)
Plan/Organize	58.61 (11.40) 41.00 – 80.00	30.43% (n = 7)
Organization of Materials	54.87 (11.04) 37.00 – 71.00	26.09% (n = 6)
Monitor	57.74 (10.22) 40.00 – 75.00	21.74% (n = 5)
Metacognition Index	59.43 (11.31) 39.00 – 81.00	34.78% (n = 8)
Global Executive Composite	57.78 (12.35) 38.00 – 80.00	30.43% (n = 7)

Note: T-scores have a mean of 50 and a standard deviation of 10. T-scores ≥ 65 on the BRIEF represent areas of significant difficulty.

For reference, the distribution of Global Executive Composite T-scores in the NF1 group is displayed in Figure 6.

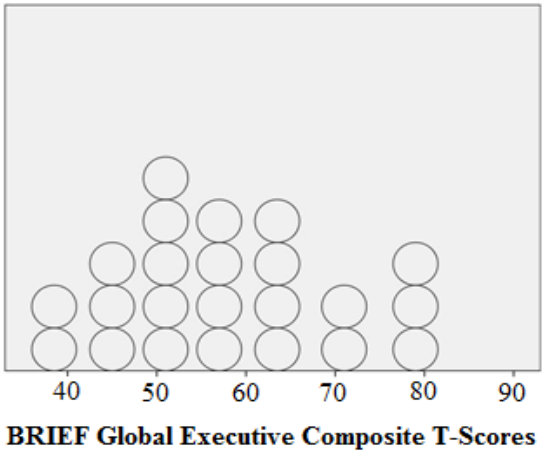

Figure 6. Dot plot showing distribution of Behavior Rating Inventory of Executive Function (BRIEF) Global Executive Composite T-scores in the NF1 group.

Correlations

Spearman's rho correlations were conducted to explore the relationships between social competence and Conners 3–PL ratings, SRS ratings, BRIEF ratings, and FSIQ. Correlations are displayed in Table 5.

Table 5

Correlations between social competence (SCPQ–P) and FSIQ, Conners 3–PL ratings, SRS ratings, and BRIEF ratings for NF1 participants.

	Spearman's correlation (ρ)	*p* value
Conners 3–PL Content Scores		
Inattention	.02	.930
Hyperactivity/Impulsivity	.19	.395
Learning Problems	-.16	.478
Executive Functioning	-.22	.317
Defiance/Aggression	.09	.693
Peer Relations	-.80	<.001**
Social Responsiveness Scale Scores		
Social Awareness	-.07	.753
Social Cognition	-.28	.191
Social Communication	-.42	.049*
Social Motivation	-.59	.003**
Autistic Mannerisms	-.42	.045*
SRS Total Score	-.43	.042*
Behavior Rating Inventory of Executive Function		
Behavior Regulation Index	-.02	.944
Metacognition Index	-.17	.452
Global Executive Composite	-.11	.612
FSIQ	.04	.870

* Correlation significant at the $p < .05$ level
** Correlation significant at the $p < .01$ level

Does social competence relate to psychopathology (ADHD and ASD symptomatology) in NF1?

The relationships between social competence and ADHD symptomatology (Conners 3–PL ratings of Inattention and Hyperactivity/ Impulsivity) and ASD symptomatology (SRS ratings) in the NF1 group were investigated. No significant associations were identified between ADHD symptoms (Inattention, Hyperactivity/Impulsivity) and SCPQ–P ratings for NF1 participants (both, $p > .395$). SCPQ–P ratings were significantly and negatively correlated with total levels of autistic symptomatology (SRS Total Score; $p = .048$) and also with the SRS Social Communication ($p = .049$), Social Motivation ($p = .003$) and Autistic Mannerisms ($p = .045$) subscales. Relationships between these variables are displayed visually in scatterplots in Figures 7, 8 and 9.

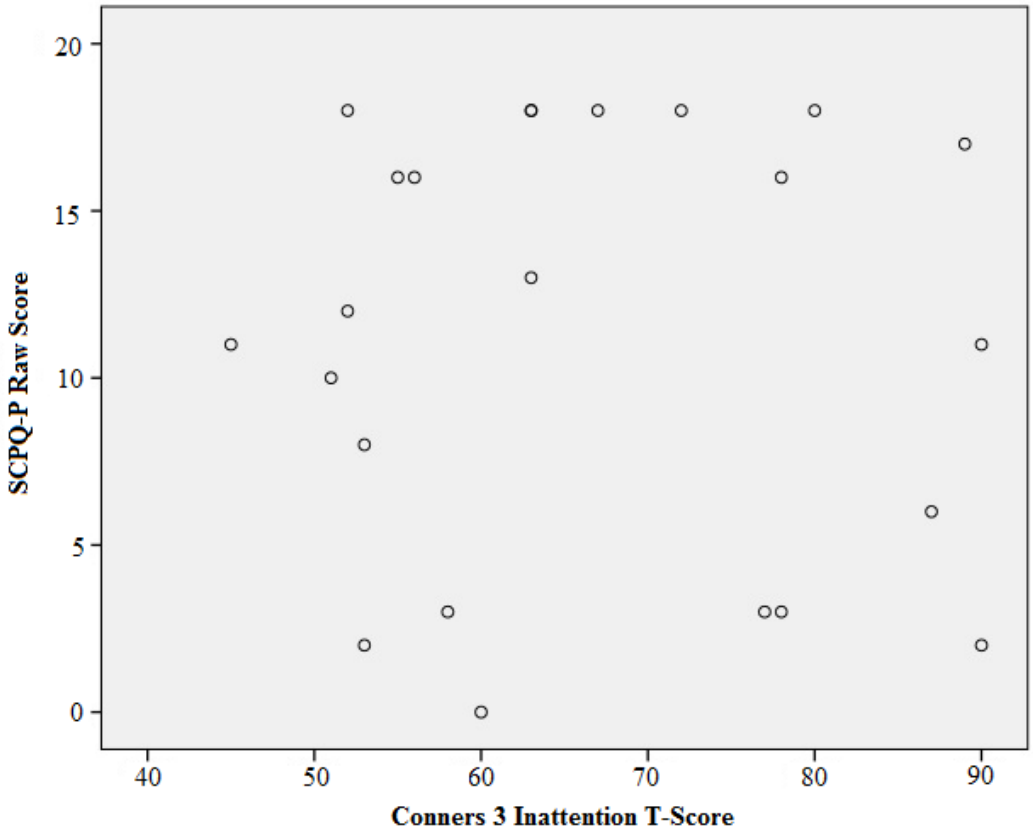

Figure 7. Scatterplot showing relationships between SCPQ–P ratings and Conners 3 Inattention T-scores in the NF1 group.

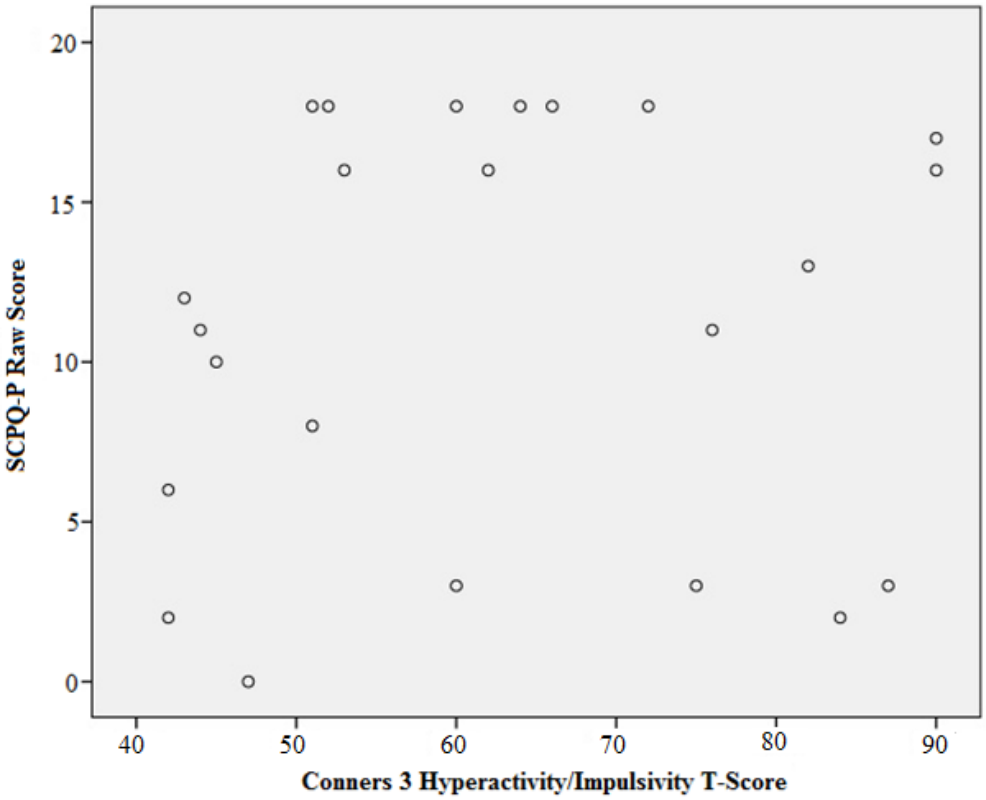

Figure 8. Scatterplot showing relationships between SCPQ–P ratings and Conners 3 Hyperactivity/Impulsivity T-scores in the NF1 group.

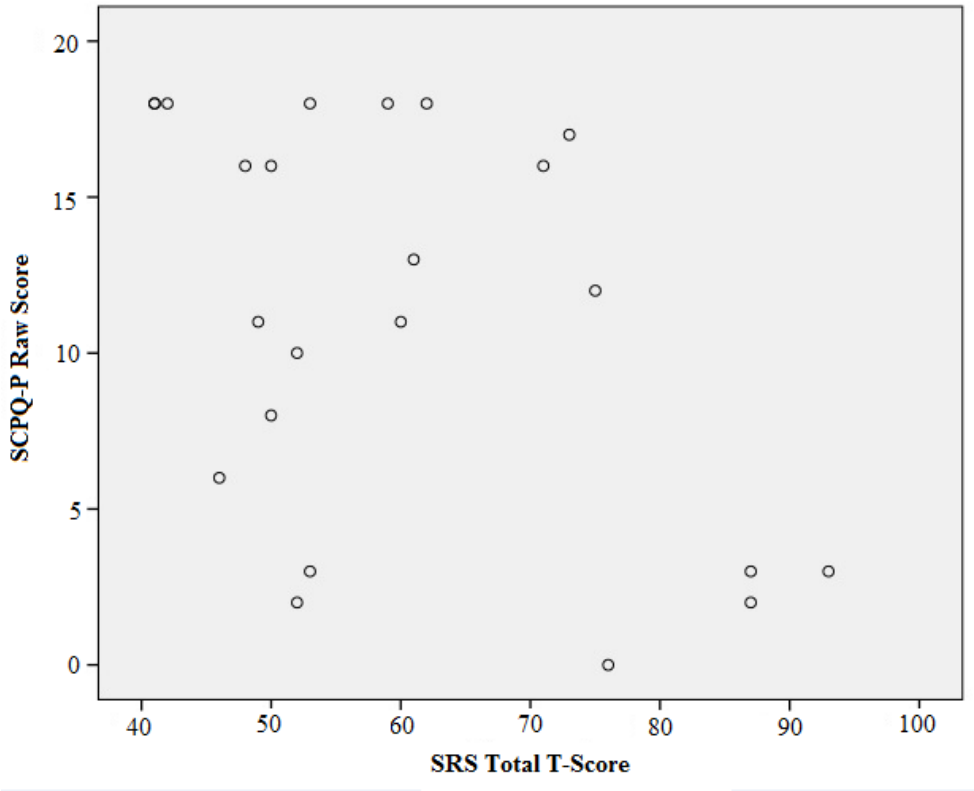

Figure 9. Scatterplot showing relationships between SCPQ–P ratings and Social Responsiveness Scale Total T-scores in the NF1 group.

Does social competence relate to cognition in NF1?

The relationships between social competence, FSIQ, and day to day executive function (BRIEF and Conners 3–PL Executive Functioning scale ratings) in the NF1 group were also investigated. SCPQ–P ratings were not significantly correlated with FSIQ (p = .870). Furthermore, SCPQ–P ratings were not significantly correlated with parent ratings of executive function on the BRIEF subscales and indices (all, $p > .05$) or the Conners 3–PL Executive Functioning content scale (all, $p > .05$).

The relationship between SCPQ–P ratings and total executive dysfunction (BRIEF Global Executive Composite T-scores) is displayed visually in a scatterplot in Figure 10 for reference.

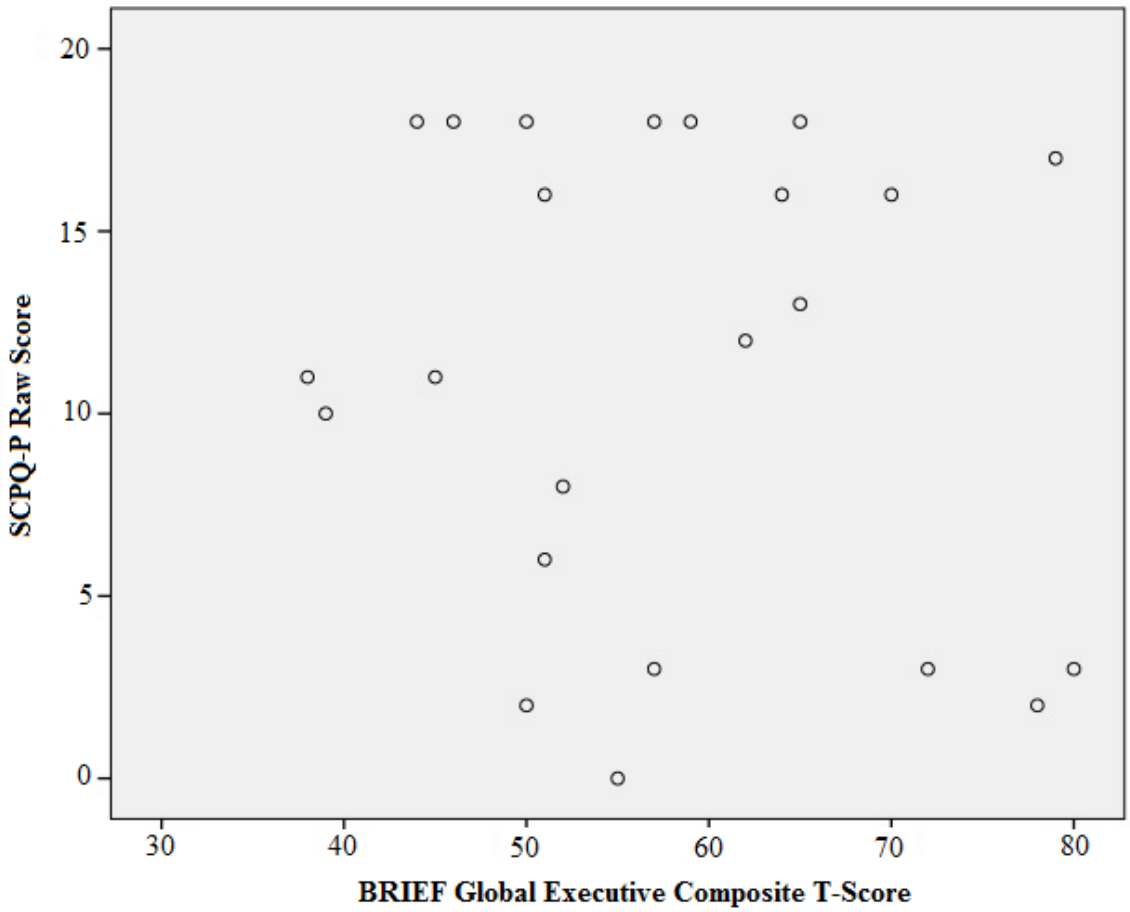

Figure 10. Scatterplot showing relationships between SCPQ–P ratings and Behavior Rating Inventory of Executive Function (BRIEF) Global Executive Composite T-scores in the NF1 group.

Discussion

The aims of this study were threefold: (1) to investigate the nature of social competence in children with NF1, (2) to explore relationships between social competence and psychopathology in NF1, and (3) to examine the relationships between social competence, cognition and behaviour in NF1. In relation to the first aim, in line with our hypothesis (Hypothesis 1), the social competence of children with NF1 differed significantly from that of typically developing children. Children with NF1 were rated by their parents as having significantly poorer overall social competence, replicating findings from previous studies using less comprehensive measures (e.g. Barton & North, 2004; Dilts et al., 1996; Noll et al. 2007). However, the present study extended existing findings by providing additional information as to the specific nature of these social competence deficits. At the group level, children with NF1 had significantly greater difficulty forming and maintaining friendships, had poorer overall relationships with their classmates, were less popular than their same-age peers, and were less likely to see friends outside of school compared with TD controls. Notably, scores on the SCPQ–P were strongly correlated with scores on the Conners 3–PL Peer Relations scale, supporting its validity as a measure of social competence for children with NF1. As predicted (Hypothesis 2), there was significantly greater individual variability in social competence ratings among children with NF1 when compared with the TD control group, with some NF1 children falling in the normal range, and others demonstrating significant impairments in day to day social competence. This indicates that some children with NF1 may be more vulnerable to social difficulties than others.

In relation to the second aim, 47.8% of NF1 children were rated as having significantly elevated inattention and/or hyperactivity symptoms. Additionally, 43.5% displayed elevated levels of autistic symptomatology and four children (17.4%) displayed severe symptoms at a level which is strongly associated with a clinical ASD diagnosis. In

total, 30.4% demonstrated clinically elevated symptoms of both ADHD and ASD. The percentage of children falling within the clinically significant range for ADHD and ASD symptoms in this study was comparable to the proportions found in previous research on NF1 (Garg, Lehtonen, et al., 2013; Hofman et al., 1994; Hyman et al., 2005; Mautner et al., 2002; Walsh et al., 2013).

As predicted (Hypothesis 3), children with NF1 and no comorbid ADHD or ASD diagnosis were rated by their parents as having significant social competence problems; group differences in social competence ratings between NF1 children and TD controls remained significant even after excluding NF1 participants with a comorbid psychological diagnosis. However, our hypothesis that social competence would be significantly related to ADHD and ASD symptomatology (Hypothesis 4) was only partially supported. Contrary to predictions, social competence was not significantly related to parent-rated levels of inattention or hyperactivity in our NF1 cohort, nor was social competence related to behavioural indices commonly associated with ADHD, such as defiance/aggression and learning problems. These findings contradict those of previous studies (e.g. Barton & North, 2004; Noll et al., 2007), which identified children with NF1 and comorbid ADHD and/or learning problems as those most at risk for social problems. Additionally, ADHD is strongly associated with social incompetence in children without NF1 (De Boo & Prins, 2007; Ronk, Hung, & Landau, 2011). Our results are somewhat surprising and may represent a cohort effect in our relatively small sample. Further study in a larger sample of children with NF1 is certainly warranted to confirm our present findings.

In keeping with expectations (Hypothesis 4), social competence was significantly associated with overall levels of ASD symptomatology in children with NF1, such that individuals with higher ASD symptom levels displayed lower overall social competence. This correlation is unsurprising as theoretically there is likely to be significant overlap between

ASD symptomatology and social outcomes and behaviour, however our findings reveal novel information about the specific symptom subscales which appear to be most associated with social competence in children with NF1. There were significant correlations between social competence and scores on the SRS Autistic Mannerisms treatment subscale (e.g. "has repetitive odd behaviours such as hand flapping or rocking," "has a restricted or unusually narrow range of interests") and Social Communication treatment subscale (e.g. "avoids eye contact or has unusual eye contact", "gets teased a lot") in the expected direction. It is also interesting to note that a large proportion of the NF1 group (43.5%) demonstrated significant difficulties with social motivation, which taps into socially anxious and avoidant behaviours (e.g. "is too tense in social settings", "avoids starting social interactions with peers or adults"). This suggests a vulnerability to symptoms of social anxiety in children with NF1 and supports previous research showing a potential predisposition for anxiety disorders in this population (Pasini et al., 2012). Social Motivation ratings were found to be significantly related to social competence, such that children experiencing increased anxious or avoidant behaviours also displayed lower social competence. Further exploration of social anxiety and its relationship to social functioning in NF1 is warranted, as this may be impacting not only on the ability to form and maintain friendships, but also on emotional and behavioural functioning and overall quality of life in this population. The pattern of results observed in the present study certainly suggests that some combination of autistic traits and social anxiety symptoms might be contributing to the social competence deficits observed in some children with NF1.

The third aim of this study was to explore the relationships between social competence, FSIQ, and executive function in children with NF1. In keeping with expectations (Hypothesis 5), social competence was not significantly related to general levels of intellectual functioning in the NF1 group. However, our hypothesis that lower social competence would be associated with higher levels of day to day executive dysfunction

(Hypothesis 6) was not supported. While group means were not significantly different from those reported in published normative data, over half (56.5%) of the children with NF1 in our cohort were rated by their parents as demonstrating difficulty at a clinically significant level in at least one executive domain, supporting previous research showing significant day to day executive dysfunction in this population (e.g. Payne et al., 2011). Previous studies have shown significant relationships between social deficits and executive dysfunction in typically developing children (Razza, 2009; Riggs et al., 2006), ASD (McEvoy, Rogers, & Pennington, 1993; Ozonoff, Pennington, & Rogers, 1991), and other genetic disorders, including 22q11 deletion syndrome (Kiley-Brabeck & Sobin, 2006), but no existing study has explicitly explored the relationship between social competence and executive function in NF1. While the lack of relationships between functional executive behaviours and social competence are not clear, one possible explanation is that our study solely relied on parent report questionnaires of executive function, which only measure children's executive abilities in the home environment and so may be less sensitive than other executive function measures. Of note, a previous study investigating the correlations between informant report measures of executive function and neuropsychological test performance in children with NF1 found inconsistent relationships between these variables, suggesting that these measures might tap different constructs (Payne et al., 2011). Future research investigating social competence and executive function in children with NF1 should supplement parent reports of executive function with additional measures, including teacher report questionnaires and behavioural assessment tools, such as the Behavioural Assessment of the Dysexecutive Syndrome in Children (BADS-C; Emslie, Wilson, Burden, Nimmo-Smith, & Wilson, 2003).

Study Limitations

There were several methodological limitations in the present study which must be considered. Firstly, as mentioned above, this study relied solely on parent report

questionnaires of social and behavioural functioning. Previous research has demonstrated considerable variations between reports from different informants on social and behavioural rating instruments (Achenbach, McConaughy, & Howell, 1987). Future research investigating social competence in NF1 should corroborate parent ratings with information from additional sources, including teachers, peers, and self-report, to limit the amount of potential bias.

The possibility of response bias must also be considered. Of the 30 sets of questionnaires sent out, only 23 were returned and it is possible that the parents of children with more comorbid symptomatology and/or greater social difficulties were those most likely to choose to participate in the present study. Nevertheless, the descriptive statistics of the 23 responders were in keeping with expectations for children with NF1, and the seven non-responders did not differ significantly from responders with respect to sample demographics.

Finally, it is important to note that the ADHD and ASD symptom questionnaires used in this study were screening tools only. No diagnostic or treatment decisions can be made on these reports alone, as all ratings require confirmation from independent sources. Although 47.8% of our NF1 cohort demonstrated symptoms of ADHD in the "very elevated" range, only 21.7% of these children had a confirmed ADHD diagnosis. Future research investigating the relationship between social competence and comorbid ADHD and ASD should aim to incorporate formal information regarding confirmed diagnostic status in a larger sample to explore more rigorously the influence of these variables on day to day social functioning. This may include a diagnostic interview such as the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Kaufman et al., 2008).

Future Research

Further research in a larger sample of children with NF1 will be necessary to confirm and extend the present findings. It is clear that children with NF1 demonstrate significant social competence problems, however, the nature of the relationships between these problems

and comorbid ADHD and/or ASD diagnoses warrants further exploration. Studies with larger sample sizes could focus on subgroup analyses based on psychological comorbidities (e.g. NF1 + ADHD, NF1 + ASD, NF1 + ADHD + ASD and NF1 only) to investigate any associated differences in social competence. As stated previously, the inclusion of diagnostic assessment tools for ADHD and ASD would be informative, as would formal screening for social anxiety symptoms. Notably, when exploring the effect of ASD on social competence, it would also be important to understand the possible mediating effect of social anxiety. This could be investigated with formal statistical analyses (for example, a multiple regression model) in a larger NF1 cohort.

There are many other variables which may be important in contributing to social competence problems in children with NF1 which were not explored in the current study. For example, children with NF1 suffer from low academic achievement (Hyman et al., 2006), cosmetic disfiguration (Rosario, 2007) and significant impairment in multiple cognitive domains, including attention and language skills (Hyman et al., 2005). These variables have all been separately associated with social dysfunction in children with mild cognitive and behavioural disabilities (Gresham & MacMillan, 1997) and certainly warrant further investigation in children with NF1. Previous research has also identified deficits in social information processing and higher-level social cognition in those with NF1 (e.g. Huijbregts et al., 2010; Pride et al., 2014) which are likely to contribute to reduced social functioning. Elucidating the potential cause(s) of the social difficulties is an important task for future research, as this information will inform more individualised clinical management and intervention recommendations for children with NF1.

Clinical Implications

The present findings indicate a significant risk of social competence problems for children with NF1, even in the absence of comorbid ADHD, reduced intellectual abilities or

functional executive difficulties. As such, these findings highlight the importance of screening for social competence problems as part of standard clinical assessment and management protocols for children with NF1. Given questionnaires such as the Social Competence with Peers Questionnaire (SCPQ; Spence, 1995) are freely available tools with sound psychometric properties that can be completed in less than five minutes, incorporating them into the clinical assessment of children with NF1 is highly feasible. The questionnaire is available in parent (SCPQ–P), teacher (SCPQ–T) and pupil (SCPQ–PU) versions which all correlate strongly in neurotypical children (Spence, 1995).

In keeping with previous research (e.g. Adviento et al., 2014; Garg, Lehtonen, et al., 2013; Hyman et al., 2005; Mautner et al., 2002; Walsh et al., 2013), we identified elevated levels of ADHD and/or ASD symptoms in a large proportion of our NF1 cohort (including high levels of socially anxious behaviour). Higher levels of ASD symptomatology and socially anxious behaviour were significantly associated with poorer social competence in children with NF1. These findings strongly suggest the need for general psychological screening in children with NF1, particularly those with reduced social competence. While ADHD screening measures such as the Conners 3 rating scales (Conners, 2008) are routinely completed as part of the clinical management of children with NF1 at CHW, the present findings suggest that children with reduced social competence should also be screened for social anxiety and elevated ASD symptoms. The Social Responsiveness Scale (SRS; Constantino, 2002) may be useful as a screening measure for ASD in children with NF1 with poor social competence, providing information about specific problematic behaviours and social skills deficits that will assist clinicians in designing and implementing appropriate interventions. Notably, the SRS also includes a Social Motivation treatment subscale that assesses socially anxious and avoidant behaviours (Constantino, 2002). The Spence

Children's Anxiety Scale (SCAS; Spence, 1997) could also be administered to children with NF1 and social competence problems as a more general screen for anxiety symptoms.

Children with NF1 who display social competence problems are likely to require interventions targeted at forming and maintaining friendships with their peers. No published studies to date have explored the effectiveness of social intervention programs for children with NF1, however our present findings suggest that it may be suitable to trial treatment interventions designed for children with ASD in an NF1 cohort. In particular, intervention with a focus on social motivation and the management of anxiety surrounding social interactions may be beneficial. Nevertheless, the significant variability observed in the clinical, neuropsychological and social phenotypes of children with NF1 indicates that their social competence problems could reflect a number of individual contributing factors and individualised intervention programs targeting particular skill deficits or problem behaviours may be necessary. Spence (2003) advocates a multimodal approach to social skills training for children with social competence problems, including: behavioural skills training (e.g. modelling, role playing, feedback, and reinforcement); social perception skills training; instruction in self-regulation techniques; social problem solving; and parent training. The development and implementation of these programs for children with NF1 will be an important task for future research.

Conclusion

The present findings indicate that children with NF1 are at significant risk of day to day social competence problems, especially those who display high levels of autistic symptomatology and socially anxious behaviour. Nevertheless, social competence problems in NF1 occur even in the absence of comorbid ADHD and ASD and do not appear to be related to general levels of intellectual functioning or functional executive abilities. These results suggest a need to incorporate assessment, prevention, and intervention for social

problems into the general clinical management of children with NF1, even for those children with relatively normal neuropsychological profiles. Identifying the contributing factors of social competence problems in NF1 and designing appropriate intervention programs will be important challenges for future research.

Author Contributions

This study was conceived by Amelia Lewis, Melanie Porter, Jonathan Payne and Kathryn North. Amelia Lewis took the leading role in collecting and analysing data and drafting the manuscript. Melanie Porter, Jonathan Payne and Tracey Williams assisted with data interpretation and revised the manuscript for intellectual content. All authors read and approved the final manuscript.

Acknowledgement of Initial Publication

The authors acknowledge that an edited version of this paper was first published online by the *Journal of Childhood and Developmental Disorders* on 21st March 2016 prior to digital submission of this thesis. Citation: Lewis AK, Porter MA, Williams TA, et al. Social Competence in Children with Neurofibromatosis Type 1: Relationships with Psychopathology and Cognitive Ability. J Child Dev Disord. 2016, 2:2.

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Appendix

Social Responsiveness Scale (SRS) Treatment Subscale Descriptions

The SRS manual (Constantino, 2002) highlights the need for a differentiated approach in the treatment of ASD. The treatment subscales on the SRS are designed to reflect the various ASD symptom clusters relating to different aspects of reciprocal social behaviour. T-scores of 60 and higher on any given subscale are considered elevated and may be significant enough to warrant specific intervention. Furthermore, differences of five T-score points or more between subscales are considered clinically significant, and may inform the levels of priority given to specific problematic behaviours or skill deficits in treatment or intervention programs. Below is a description of the behavioural observations represented in each of the five subscales.

Social Awareness:

The Social Awareness subscale assesses a child's ability to recognise social cues. Items include things like "walks in between two people who are talking" and "is aware of what others are thinking or feeling".

Social Cognition:

The Social Cognition subscale assesses a child's ability to interpret social cues once they have been picked up. Items include things like "is overly suspicious" and "takes things too literally and doesn't get the real meaning of a conversation".

Social Communication:

The Social Communication subscale assesses a child's expressive social communication skills. Items include things like "has difficulty relating to peers", "gets teased a lot", and "avoids eye contact or has unusual eye contact".

Social Motivation:

The Social Motivation subscale assesses a child's willingness and motivation to engage in social interactions, including elements of social anxiety, inhibition, and empathic orientation. Items include "is too tense in social settings", "avoids starting social interactions with peers or adults", and "does not join group activities unless told to do so".

Autistic Mannerisms:

The Autistic Mannerisms subscale assesses the stereotypical behaviours or restricted interests characteristic of children with an ASD. Items include "has an unusually narrow range of interests" and "has repetitive, odd behaviours such as hand flapping or rocking".

PAPER 2

Facial Emotion Recognition, Face Scan Paths, and Face Perception in Children with Neurofibromatosis Type 1

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Abstract

This study investigated facial emotion recognition, face scan paths (time spent viewing different facial features) and face perception (the ability to discriminate between and match physical characteristics of faces) in 29 children with neurofibromatosis type 1 (NF1) compared to 29 chronological age-matched typically developing controls. The relationships between facial emotion recognition, face scan paths, face perception and social competence in children with NF1 were also examined. Results indicated that children with NF1 displayed significantly poorer recognition of fearful expressions compared to controls, as well as a non-significant trend towards poorer recognition of anger. While there was no significant difference between groups in time spent viewing individual core facial features (eyes, nose, mouth and non-feature regions), children with NF1 spent significantly less time than controls viewing the face as a whole. Children with NF1 also displayed significantly poorer face perception abilities than typically developing controls. Facial emotion recognition deficits were not significantly associated with time spent viewing facial features, social competence problems or face perception abilities in the NF1 group, although a non-significant trend was observed whereby better recognition of anger was associated with increased face perception accuracy. These results have important implications for the clinical management of children with NF1.

Key Words: NF1, emotion recognition, scan paths, face perception.

Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by a mutation of the NF1 gene on the long arm of chromosome 17 (Yohay, 2006). The most common complications of the condition include cognitive impairment (e.g. Hyman, Shores, & North, 2005; Levine, Materek, Abel, O'Donnell, & Cutting, 2006) and psychopathology (e.g. Garg et al., 2013; Johnson, Saal, Lovell, & Schorry, 1999; Walsh et al., 2013). Social dysfunction is also widespread amongst both adults and children with NF1 (Barton & North, 2004; Huijbregts & De Sonneville, 2011; Noll et al., 2007; Pride, Crawford, Payne, & North, 2013). Two recent studies have revealed specific facial emotion recognition deficits in children and adults with NF1 (Huijbregts, Jahja, De Sonneville, De Breij, & Swaab-Barneveld, 2010; Pride et al., 2014), which might underlie some of the social difficulties observed in this population. Nevertheless, the mechanism(s) underlying emotion recognition problems in individuals with NF1 remain unclear. Pride et al. (2014) speculated that facial emotion recognition deficits in NF1 might reflect aberrant visual scanning of facial features or, alternatively, more general deficits in face perception. However, no study to date has directly investigated relationships between face scan paths, face perception and emotion recognition skills in individuals with NF1. As such, the primary aims of the present study were to further establish the presence of facial emotion recognition problems in children with NF1 – especially for anger and fear – and to investigate whether these emotion recognition skills are related to visual scanning of faces (time spent viewing individual facial features) and/or face perception abilities (the ability to discriminate between and match physical characteristics of faces) in this cohort. The relationships between facial emotion recognition, face perception and day to day social competence were also explored in our cohort of children with NF1.

Only one study to date has directly examined facial emotion recognition skills in a paediatric NF1 cohort. Huijbregts et al. (2010) investigated emotion recognition skills in children and adolescents with NF1 using computerised tests from the Amsterdam Neuropsychological Tasks battery (De Sonneville, 1999). On a forced choice matching task, children with NF1 displayed significantly poorer recognition accuracy for fearful facial expressions, but not for expressions of happiness, sadness or anger, compared to controls. Furthermore, in an additional task requiring participants to indicate whether two pictures presented simultaneously on a screen displayed the same emotion, children with NF1 were significantly less accurate in identifying pairs of fearful and angry facial expressions. Group differences in recognition accuracy remained when performances on cognitive control tasks (inhibition and working memory measures) were covaried. Taken together, the above findings indicate difficulty identifying expressions of fear and anger in children with NF1.

In the same study, Huijbregts et al. (2010) investigated face recognition skills and their NF1 group was found to be impaired, on average, compared to controls. Unfortunately, the relationship between face recognition and emotion recognition abilities was not explored statistically. Specifically, results revealed that children with NF1 were less accurate than controls in recognising whether or not a target face stimulus presented in profile view appeared in a subsequent response set of four photographs, although this effect appeared to be driven primarily by the younger children (those aged 12 years and under) in the study. Children with NF1 were also significantly slower to recognise faces compared to control children when presented in both frontal and profile views. All group differences failed to reach significance when performances on cognitive control (inhibition and working memory) tasks were taken into account, supporting the authors' hypothesis that deficits in top-down cognitive processes contribute to face recognition deficits in children with NF1. Notably, however, the face recognition task employed in this study involved a visual working memory

component, as well as a face discrimination component and so the mechanisms underlying the performance deficits evident in children with NF1 remain unclear. In particular, it remains to be seen whether children with NF1 demonstrate specific impairments in the perceptual discrimination and matching of faces and whether or not these abilities are related to facial emotion recognition skills in this population (we refer to this as 'face perception' in the present study).

In a more recent study, Pride and colleagues (2014) examined social cognition and emotion recognition skills in adults with NF1 using The Awareness of Social Inference Test (TASIT; McDonald, Flanagan, Rollins, & Kinch, 2003) and used volumetric magnetic resonance imaging analyses to explore the neuroanatomical basis of social cognitive deficits in this population. For the emotion recognition portion of the TASIT, participants were required to watch brief video vignettes of an actor and were asked to identify the emotion portrayed (neutral, happy, sad, angry, disgusted, fearful, or surprised) in a forced choice recognition format. On this task, adults with NF1 displayed significantly poorer recognition of anger compared to healthy controls. Contrary to expectations, correlational analyses in the NF1 group failed to reveal a significant relationship between emotion recognition performance and total grey matter volume in the amygdala, a region strongly associated with negative emotion processing in neurotypical individuals and other clinical populations (e.g. Adams, Gordon, Baird, Ambady, & Kleck, 2003; Phan, Fitzgerald, Nathan, & Tancer, 2006; Whalen et al., 2001). Nevertheless, a non-significant trend was observed whereby larger grey matter volume in the left fusiform gyrus was associated with poorer overall emotion recognition in those with NF1. As the fusiform gyrus is a key region subserving human face detection (Grill-Spector, Knouf, & Kanwisher, 2004; McCarthy, Puce, Gore, & Allison, 1997), the authors proposed that these findings suggest the specific emotion recognition deficits in those with NF1 might be related to more general deficits in face perception.

An alternate, though related, explanation for the emotion recognition problems observed in those with NF1 is that these individuals do not visually scan faces in the same manner as neurotypical individuals. Specifically, Pride et al. (2014) speculated that individuals with NF1 may spend less time visually scanning the core facial features which provide information about facial emotional expressions. Notably, face scan path abnormalities have been identified in several neurodevelopmental and anxiety disorders characterised by impaired emotion recognition, including autism spectrum disorder (e.g. Corden, Chilvers, & Skuse, 2008; Pelphrey et al., 2002) and social phobia (e.g. Horley, Williams, Gonsalvez, & Gordon, 2003; Horley, Williams, Gonsalvez, & Gordon, 2004). No study to date has employed eye-tracking technology to investigate face scan paths in individuals with NF1.

A growing body of empirical research supports the primary importance of the eye region in face processing, particularly for negative emotional expressions. For example, Schurgin et al. (2014) used eye-tracking technology to examine the initial face scanning patterns of 51 neurotypical adults during an emotional judgment task and found that participants spent significantly more time fixating on the eye region compared to other core facial features for facial expressions of anger, fear, sadness and shame, but not for expressions of joy and disgust. The authors reported that these scanning patterns tended to reflect gaze orientation towards facial features with more 'diagnostic value' for each emotion (Schurgin et al., 2014). In keeping with these findings, several studies from both adult and paediatric populations have shown that the ability to recognise facial expressions of negative emotions is mediated by attention to the eyes and brow region, particularly for expressions of anger and fear (e.g. Adolphs et al., 2005; Bridgman et al., 2014; Dadds et al., 2006). Although speculative, the selective nature of the emotion recognition deficits previously documented in children with NF1 (that is, difficulty identifying anger and fear) would be consistent with difficulty attending to and/or processing information from the eye region.

Hypotheses

The mechanisms underlying facial emotion recognition difficulties in children with NF1 remain unclear. Limited available research suggests that abnormalities in visual scan paths and/or face perception could be contributing factors. As such, the primary aims of the present study were to further establish the presence of facial emotion recognition deficits in children with NF1 (particularly for negative emotions) and to investigate the relationships between emotion recognition, face scan paths, and face perception in this condition. Additionally, as NF1 is associated with significantly higher rates of Attention Deficit Hyperactivity Disorder (ADHD) compared to the general population (Hyman et al., 2005; Mautner, Kluwe, Thakker, & Leark, 2002), and ADHD itself has been associated with face processing abnormalities in the absence of NF1 (Marsh, 2008), the relationships between ADHD symptomatology and our variables of interest were explored in our clinical sample. In light of the literature detailed above, it was hypothesised that, compared to typically developing controls, children with NF1 would display: poorer recognition of fearful and angry facial expressions (Hypothesis 1); aberrant face scan paths, with less time spent viewing core facial features, in particular the eye region (Hypothesis 2); and poorer face perception on a face discrimination and matching task (Hypothesis 3). It was also hypothesised that emotion recognition deficits in children with NF1 would be related to both less time spent viewing core facial features (Hypothesis 4) and poor face recognition (Hypothesis 5).

No studies to date have investigated whether emotion recognition deficits in NF1 are associated with day to day social dysfunction in this population. Although impairments in social skills and social competence have been well documented in children with NF1 (Barton & North, 2004; Dilts et al., 1996; Lewis, Porter, Payne, & Williams, in prep; Noll et al., 2007), the factors contributing to their social difficulties remain unclear. This information

would assist education and health professionals in providing targeted intervention recommendations. As such, a secondary aim of this study was to investigate whether emotion recognition deficits and face perception problems were associated with daily social competence problems in children with NF1. It was hypothesised that in the NF1 group, poorer day to day social competence would be associated with (a) poorer emotion recognition skills and (b) poorer face perception (Hypothesis 6). These relationships were not explored in typically developing children, as it was assumed that they would not display sufficient variability in their social competence ratings or other scores to facilitate correlational analyses.

Method

Participants

Participants were 29 individuals with NF1 (9 males, 20 females) aged between 6 and 13 years and 29 typically developing (TD) controls (16 males, 13 females)[7]. The NF1 and TD groups were individually matched for chronological age (within 6 months of age). All participants displayed normal or corrected to normal vision. Table 1 displays the demographic characteristics of each group. As shown in Table 1, a chi-square test revealed no significant difference in handedness or sex distribution between the groups, although a trend was observed whereby there were more females in the NF1 group. Independent samples *t* test confirmed that the two groups were well matched in terms of age (see Table 1). Consistent with the literature showing downward shifts in FSIQ in NF1 (Feldmann, Denecke, Grenzebach, Schuierer, & Weglage, 2003; Ferner, Hughes, & Weinman, 1996; Hyman et al., 2005), the two groups differed significantly in terms of their FSIQ scores, albeit on different

[7] We originally recruited 30 NF1 participants however one did not meet all inclusion criteria and was subsequently excluded.

measurement instruments (see Table 1). On average, the NF1 group fell within the low average IQ range and the TD control group fell within the average IQ range[8].

Table 1

Demographic characteristics for each group.

	NF1 group ***Mean (SD)*** *Range*	TD group ***Mean (SD)*** *Range*	*t* score	*p* value
Males : Females	9 : 20	16 : 13	3.445 ˆ	.063
Right-Handed : Left-Handed	27 : 2	26 : 3	.219 ˆ	.640
Chronological Age	**10.15 (1.99)** 6.67 – 13.83	**10.10 (2.09)** 6.67 – 13.42	.080	.937
FSIQ	**88.86 (10.31)**[a] 71.00 – 109.00	**105.38 (11.84)**[b] 79.00 – 125.00	-5.666	< .001

ˆ Chi-square statistic
[a] FSIQ measured using WISC-IV
[b] FSIQ measured using WASI
Note: Age is in years. FSIQ scores from both the WISC-IV and WASI are standardised against a normative mean of 100.00 and a standard deviation of 15.00.

NF1 Participants

NF1 participants in this study were recruited through the Neurogenetics Clinic at The Children's Hospital at Westmead (CHW), Sydney, Australia. This clinic has a wide referral base and services over 1300 individuals with NF1, with all socioeconomic groups represented. Children were required to meet the following inclusion criteria: (a) confirmed diagnosis of NF1 based on criteria specified by the National Institutes of Health Consensus Conference (NIH, 1988), (b) absence of diagnosed symptomatic intracranial pathology (such as epilepsy, traumatic brain injury, or brain tumour), (c) IQ ≥ 70, (d) no current or previous diagnosis of anxiety, mood, or psychotic disorder(s), and (e) competency in the English language. One NF1 participant failed to meet criterion (c) and was excluded. Clinical review revealed that six NF1 participants had a comorbid diagnosis of ADHD. For NF1 participants,

[8] To investigate relationships between FSIQ and the variables analysed in the present study, non-parametric (Spearman's rho) correlations were conducted between all variables both groups. In the NF1 group, FSIQ was significantly associated with gender ($p = .040$) such that females displayed higher FSIQs than males. There were no significant relationships between FSIQ and emotion recognition (all, $p \geq .129$), scan path parameters (all, $p \geq .177$) or face perception ($p = .053$) in the NF1 group. In the TD group, FSIQ was again significantly associated with gender ($p = .034$) such that females displayed higher IQs than males. Higher FSIQ was also significantly associated with better total emotion recognition accuracy ($p = .017$) and specifically with better recognition of anger ($p < .001$). There were no significant relationships between FSIQ and face scan paths (all, $p \geq .442$) or face perception ($p = .076$) in the TD group.

Full Scale IQ (FSIQ) was established using the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2003).

Typically Developing Controls

Typically developing (TD) controls were recruited through Neuronauts, a science club for children at Macquarie University, Sydney, Australia. TD participants were excluded from the study if they had a history of developmental delay, intellectual or cognitive disability, sensory impairments, neurological disorders, psychological or psychiatric disorders, or English as a second language. No TD controls had to be excluded based on these criteria. For TD control participants, FSIQ was estimated using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999).

Materials

Face Stimuli

Face stimuli for both eye-tracking and emotion recognition tasks were six identities from the Ekman standardised face set (IDs 1, 2, 7, 8, 9, and 13; Ekman & Friesen, 2003). These stimuli were selected as they have been identified as reliable representations of individual expressions of emotion (Palermo & Coltheart, 2004). The neutral, angry, fearful, and happy facial expressions for each of the six identities selected were used as face stimuli, resulting in a total of 24 face presentations. An equal number of male and female face stimuli were included.

Facial Recognition Test – Long Form (FRT)

The FRT (Benton, Sivan, Hamsher, Varney, & Spreen, 1994) is a standard neuropsychological measure of face perception skills designed to assess the examinee's ability to identify and discriminate photographs of unfamiliar human faces. The test is self-paced and is made up of 54 response items in which the examinee is required to match front-view photographs of faces with identical front-view faces, three quarter faces, and faces under

different lighting conditions. There is no memory component to this task as the target and response stimuli are presented simultaneously. In the present study, raw scores were converted into standardised Z-scores based on age norms reported by Paquier et al. (1999)[9]. The psychometric properties of the FRT are acceptable, although fall below the level recommended for diagnostic use (Strauss, Sherman, & Spreen, 2006), with a reported internal consistency reliability coefficient of 0.71 in a sample of older adults (Christensen, Riley, Heffernan, Love, & McLaughlin Sta. Maria, 2002).

Conners 3 – Parent Long Form (Conners 3–PL)

The Conners 3–PL (Conners, 2008) was administered to parents of children in the NF1 group as a screen for symptoms of ADHD. This standardised, commercially available measure is made up of 105 items which contribute to six content scales: Inattention, Hyperactivity/Impulsivity, Learning Problems, Executive Functioning, Defiance/Aggression, and Peer Relations. Items are rated on a four-point Likert scale from 0 (not at all true) to 3 (very much true), with higher scores indicating greater difficulty. Raw scores are then converted into T-scores using age and gender norms. Data were missing for four NF1 participants in the present study due to their informants failing to return the questionnaire.

Social Competence with Peers Questionnaire – Parent Form (SCPQ–P)

Social competence in the NF1 group was assessed using the SCPQ–P (Spence, 1995), a nine item parent questionnaire addressing the quality and quantity of children's friendships, perceived popularity, the nature of their relationships with children of the same age, and their involvement in social activities (e.g. being invited to parties and seeing friends at weekends). Items are rated on a three-point Likert scale from 0 (not true) to 2 (mostly true), with higher scores indicating greater social competence. The psychometric properties of this scale are respectable, with a reported Guttman split-half reliability coefficient of 0.87 and coefficient

[9] Paquier et al. (1999) published norms for typically developing children aged between 7 and 14 years. For the 6-year-old participants in the present study, Z-scores were generated based on 7-year-old age norms.

alpha of 0.81 (Spence, 1995). There were missing data for six NF1 participants due to informants failing to return the questionnaire.

Procedure

Participants were seated in a darkened room and viewed images on a Dell 16" FP monitor. Images were presented in the centre of the computer screen at a standardized size of 10.5cm (406 pixels) x 16.0cm (599 pixels), width by height.

Participants first viewed the face stimuli passively while their scan paths were recorded, and then completed the emotion recognition task without eye movement recordings. Similar "passive viewing" gaze recording methods have been employed in previous studies investigating visual scanning and emotion recognition skills in other clinical populations (e.g. Pelphrey et al., 2002; Porter, Shaw, & Marsh, 2010; Shaw & Porter, 2013), as research has demonstrated that visual scanning behaviour can be significantly impacted by the addition of a cognitive task (e.g. Hayhoe & Ballard, 2005; Land, 2009). As such, it was assumed that, for the purposes of the present study, passive viewing recordings would provide more accurate and naturalistic scan path information compared with scan path recordings made during the emotion recognition task.

The eye-tracking and emotion recognition tasks were completed in a single testing session along with the Facial Recognition Test and intelligence measures. Sessions lasted approximately 90 minutes for each participant, including short breaks.

Eye-Tracking Procedure

A remote Eyelink 1000 (SR-Research Ltd.) recorded participants' free eye movements at a sampling rate of 500 Hz. For most participants, calibration, validation, and subsequent eye movement recordings were made for the right eye. If calibration for the right eye was unsuccessful, the calibration procedure was repeated for the left eye and subsequent eye

movement recordings were made for the left eye. Left eye recordings were required for two NF1 participants and one TD control participant.

A nine point calibration method was used to calibrate and validate participants' eye movements prior to commencing eye-tracking trials. A centrally placed black dot (10mm in diameter) with a white centre (2mm in diameter) appeared in the centre of the screen and moved to eight locations around the periphery and centre of the screen. Participants were instructed to fixate on this dot and to follow its movements with their eyes. When participants had fixated on the dot for at least 1000 ms, the dot moved to a new location. The experimental procedure only commenced once a satisfactory calibration was achieved, such that a robust and accurate fixation recording could be obtained at any point on the computer screen. For two NF1 participants, adequate calibration could not be achieved and so scan path data were not recorded.

To control for the initial point of retinal attention, a black dot was presented in the centre of the screen for 1000 ms immediately prior to each face presentation. Participants were not able to progress to the next trial until they had fixated continuously on this central dot for 2000 ms. Once an adequate central fixation was recorded, manual experimenter control initiated the next trial, and the central fixation dot disappeared and was replaced by a face stimulus. This ensured that all participants were attending to the centre of the screen as soon as the image appeared. The central fixation dot re-appeared in between each trial.

Face stimuli were viewed passively in a pseudo-random order for 10,000 ms each. The 10,000 ms exposure time was selected to ensure there was sufficient time to investigate scan path patterns for all scan path parameters and facial features of interest, as in previous research (e.g. Shaw & Porter, 2013).

Areas of Interest

Areas of interest were traced for each face using the Eyelink Data Viewer freehand drawing function. For all 24 faces, six areas of interest were designated, including 'left eye', 'right eye', 'brow', 'nose', 'mouth', and 'non-feature' facial regions (that is, the whole face traced around the hairline minus the other 'feature' interest areas). As we were primarily interested in attendance to the eyes as a whole, data over the 'left eye', 'right eye', and 'brow' regions were summed to create a general 'eye region'[10].

Visual Scan Path Parameters

Visual scan path parameters selected for analysis included: (1) Mean Dwell Time Percent (MDTP; mean percentage of time spent attending to an area of interest relative to the total time spent attending to the screen) and (2) Mean Fixation Percent (MFP; mean percentage of fixations made within a defined area of interest). As in previous studies (e.g. Shaw & Porter, 2013; Porter et al., 2010), similar patterns of results were found for MDTP and MFP, so only the former is reported here.

Emotion Recognition Procedure

The same images used in the visual scan path experiment were re-presented in the same pseudo-randomised order. For each item, participants were instructed to verbally label the expression displayed on the screen in a forced choice response format (*"Do you think this expression is 'happy', 'scared', 'angry', or 'neutral'?"*). It was explained that 'neutral' means 'no emotion'. Participants were given an unlimited time to respond. The image remained on the screen until a verbal response was made and manual experimenter control initiated the next trial.

[10] Between-group ANOVAs comparing mean dwell time percent (MDTP) and mean fixation percent (MFP) to the left eye, right eye, and brow revealed no significant differences (all, $p > .05$).

Statistical Analysis

Data were analysed using Predictive Analytics SoftWare (PASW) Statistics Version 18 for Windows.

Results

A *p* value of 0.05 was used to indicate statistical significance. Bonferroni corrections were made for multiple comparisons as appropriate to reduce the likelihood of Type I error.

Do children with NF1 demonstrate specific emotion recognition deficits?

To test for group differences in emotion recognition skills, we had intended to run a repeated measures analysis of variance (ANOVA) on mean emotion recognition accuracy (mean percent correct) with Group (NF1, TD) as the between-subjects factor and Emotion (neutral, angry, fearful, and happy) as the within-subjects factor. However, all participants performed at ceiling in their recognition of happy facial expressions, so this emotion had to be excluded from subsequent analyses. Furthermore, investigations revealed that the emotion recognition data were not normally distributed with problematic skew. As such, we conducted separate non-parametric Mann-Whitney U tests to investigate whether there was any difference between the NF1 and TD groups in emotion recognition accuracy for neutral, angry and fearful facial expressions (α = .017 with Bonferroni correction).

Mann-Whitney U test revealed a significant group difference in recognition accuracy for fearful facial expressions (Z = -2.53, p = .011, r = 0.33), such that, on average, the NF1 group demonstrated significantly poorer recognition accuracy for fearful expressions than the TD group. There were no significant group differences in recognition accuracy for neutral expressions (Z = -.82, p = .410, r = 0.11) or angry expressions (Z = -1.91, p = .056, r = 0.25), although a trend was observed whereby the NF1 group displayed poorer recognition accuracy for angry facial expressions compared to controls. These results are displayed in Figure 1.

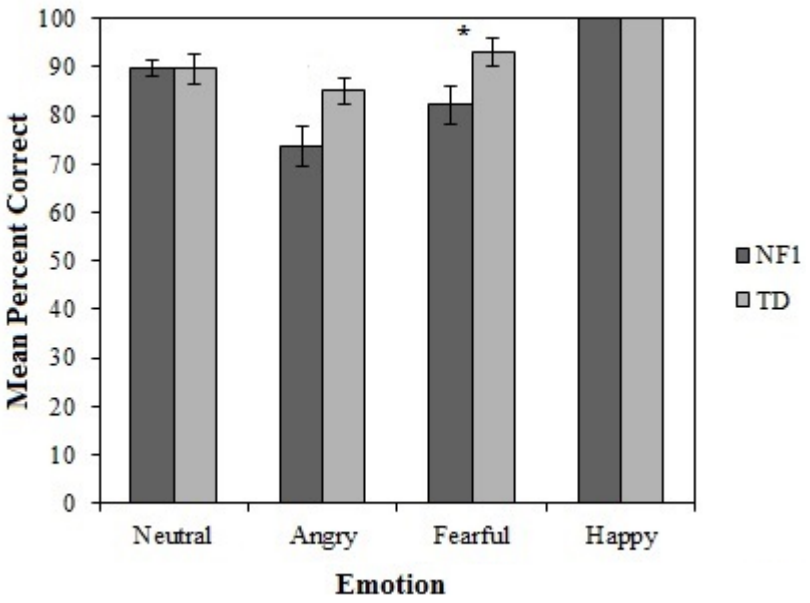

Figure 1. Mean emotion recognition accuracy scores (percent correct) for NF1 and TD control groups across all four emotions. Error bars represent +/- 1 standard error. * = $p < .017$.

To investigate the relationships between our variables of interest and ADHD symptomatology in our NF1 sample, non-parametric (Spearman's rho) correlations were conducted between all variables of interest and Conners 3–PL ratings of Inattention (M = 67.32, SD = 14.00) and Hyperactivity/Impulsivity (M = 62.76, SD = 15.89) in the NF1 group. Correlations failed to detect significant relationships between emotion recognition accuracy and Inattention (all, $p \geq .290$) or Hyperactivity/Impulsivity (all, $p \geq .502$) in the NF1 group.

Given the uneven male:female ratio in the present study, Spearman's rho correlations between gender and emotion recognition skills were examined for the NF1 and TD control groups to address the possibility of bias due to gender effects. In the NF1 group, there were no significant relationships between gender and emotion recognition accuracy (all, $p \geq .276$). In the TD control group, females demonstrated significantly better recognition accuracy for anger ($\rho = .435$, $p = .018$) than males, but there were no significant relationships between gender and recognition of other emotional expressions (all, $p \geq .132$).

Do children with NF1 do spend less time viewing individual core facial features?

To test for group differences in MDTP across different facial features a repeated measures ANOVA was conducted with Group (NF1, TD) as the between-subjects factor and Interest Area (eye region, nose, mouth, non-feature) as the within-subjects factor. Mauchly's test of sphericity indicated that the assumption of sphericity had been violated [$\chi^2_{(5)} = 23.42$, $p < .001$], so degrees of freedom were corrected using the Huynh-Feldt estimates of sphericity (epsilon = .808) to reduce the possibility of Type I error. Results revealed a significant main effect for Group [$F_{(1, 54)} = 4.62$, $p = .036$, $\eta^2 = 0.08$], such that, on average, the NF1 group spent less time viewing the face as a whole (i.e. less time dwelling in all interest areas) compared with TD controls. There was also a significant main effect for Interest Area [$F_{(2.43, 130.95)} = 48.50$, $p < .001$, $\eta^2 = 0.47$]. Post-hoc contrasts revealed that the main effect of Interest Area was explained by significantly smaller MDTP to non-feature facial regions (all, $p < .001$) and the significantly larger MDTP to the eye region (all, $p < .001$) compared to other interest areas. There was no significant Group x Interest Area interaction [$F_{(2.43, 130.95)} = 1.57$, $p = .207$, $\eta^2 = 0.02$], suggesting that the NF1 group did not differ significantly from TD controls in MDTP to each individual Interest Area. These results are displayed in Figure 2.

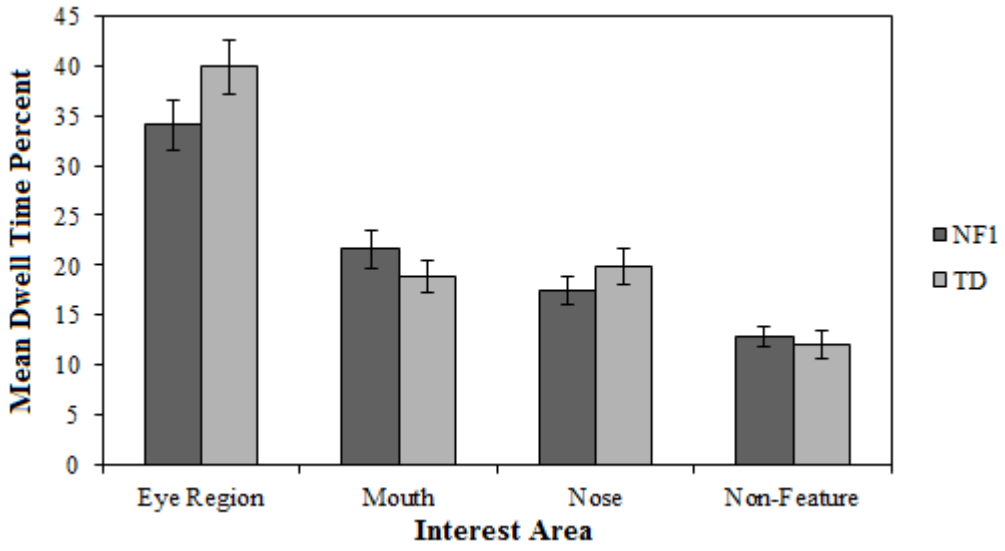

Figure 2. MDTP across each Interest Area for NF1 and TD control groups. Error bars represent +/- 1 standard error.

To investigate further the relationship between comorbid ADHD and MDTP to the face as a whole, a composite score labelled "MDTP to whole face" was generated by summing MDTP scores across the eye region, nose, mouth, and non-feature facial regions. We then generated a dot plot displaying the distribution of MDTP to whole face scores for participants in the NF1 group with and without comorbid ADHD diagnoses. These data are displayed in Figure 3.

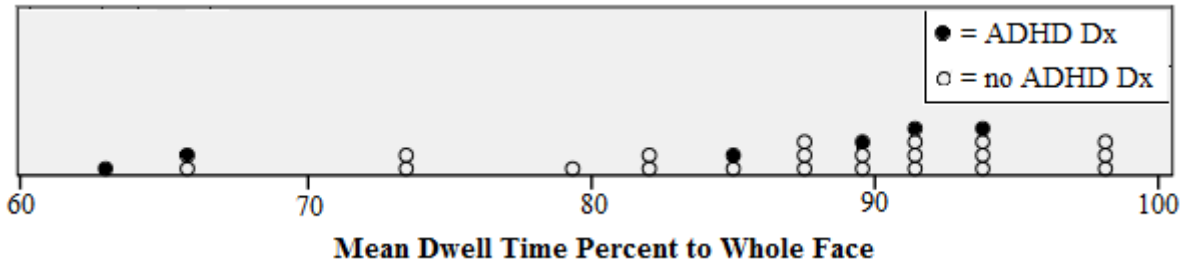

Figure 3. Dot plot showing MDTP to the whole face for participants with and without comorbid ADHD diagnoses.

Spearman's rho correlations were also examined between MDTP to the whole face and ADHD symptomatology in the NF1 group. Correlations failed to detect any significant relationships between time spent viewing the whole face and parent ratings of Inattention (ρ = -.195, p = .373) or Hyperactivity/Impulsivity (ρ = .015, p = .946) in our clinical sample.

Do children with NF1 spend less time viewing the eye region of angry and fearful facial expressions?

To investigate whether children with NF1 spent less time than TD controls viewing the eye region for fearful facial expressions, a repeated measures ANOVA was conducted on MDTP to the eye region with Group (NF1, TD) as the between-subjects factor and Emotion (neutral, angry, fearful, happy) as the within-subjects factor. Results revealed a significant main effect for Emotion [$F_{(3, 162)}$ = 16.94, p < .001, , η^2 = 0.24], but no significant main effect for Group [$F_{(1, 54)}$ = 2.49, p = .120, η^2 = 0.04]. The main effect of Emotion was explained by significantly smaller MDTP to the eye region for happy expressions compared with all other

emotions (all, $p \leq .003$) across groups. There was no significant Group x Emotion interaction [$F_{(3, 162)} = 0.85$, $p = .467$, $\eta^2 = 0.01$], indicating that the NF1 group spent similar percentages of viewing time dwelling in the eye region to TD controls, regardless of emotion. These results are displayed in Figure 3.

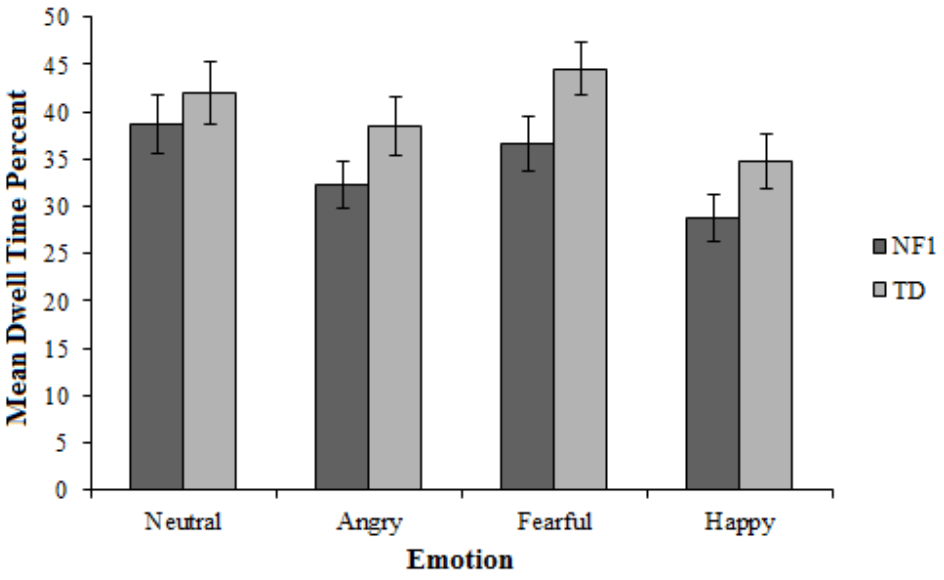

Figure 3. MDTP to the eye region for NF1 and TD control groups across each emotion. Error bars represent +/- 1 standard error.

To investigate the relationships between ADHD symptomatology and scan path parameters, Spearman's rho correlations between scan path parameters and Conners 3–PL ratings of Inattention and Hyperactivity/Impulsivity were examined in the NF1 group. Correlational analyses failed to detect any significant relationships between scan path parameters and Inattention (all, $p \geq .220$) or Hyperactivity/Impulsivity (all, $p \geq .318$) in our clinical sample.

There were no significant relationships between gender and any scan path parameters in the NF1 or TD control groups (all, $p \geq .113$).

Do children with NF1 display face perception deficits?

Table 2 displays the mean raw scores on the Facial Recognition Test for the NF1 and TD control groups. An independent samples *t* test revealed that the NF1 group performed

significantly worse than the TD group on this measure ($p < .001$, $r = 0.52$), suggesting that, on average, the NF1 group displayed significantly poorer face perception abilities than the TD group.

Table 2

Mean raw scores for the Facial Recognition Test – Long Form for both groups.

	NF1 group ***Mean (SD)*** *Range*	TD group ***Mean (SD)*** *Range*	*t* score	*p* value
Facial Recognition Test	**35.76 (4.84)** 25.00 – 45.00	**40.69 (3.26)** 35.00 – 47.00	-4.550	<.001

Note: Table 2 displays mean FRT raw scores (maximum score = 54).

To investigate the percentage of participants from each group scoring within the impaired range on the FRT, age-adjusted Z-scores were also generated for all participants based on age norms reported by Paquier et al. (1999). "Impairment" was defined as a Z-score ≤ 1.5 (that is, a score 1.5 or more standard deviations below the normative mean). No TD controls (0.0%) and seven participants in the NF1 group (24.1%) performed within the impaired range on the FRT. Three of those seven NF1 participants with impaired FRT performances also had comorbid ADHD diagnoses.

To investigate the relationships between face perception skills and ADHD symptomatology in the NF1 group, Spearman's rho correlations were conducted between age-adjusted FRT Z-scores and Conners 3–PL ratings of Inattention and Hyperactivity/Impulsivity. Correlational analyses failed to detect significant relationships between face perception skills and Inattention ($\rho = .138$, $p = .509$) or Hyperactivity/Impulsivity ($\rho = .223$, $p = .283$) in the NF1 group.

Again, to address the possibility of bias due to gender effects on face perception, non-parametric (Spearman's rho) correlations between gender and age-adjusted FRT Z-scores were conducted for the NF1 and TD control groups. In the NF1 group, there was a significant relationship between gender and face perception, such that females demonstrated significantly

better face perception compared to males (ρ = .379, p = .043). There was no significant relationship between gender and face perception in the TD control group (ρ =.232, p = .225).

Are emotion recognition deficits in NF1 related to time spent viewing facial features?

To investigate the relationships between emotion recognition problems and scan path parameters in children with NF1, non-parametric correlational analyses (Spearman's rho correlations) were conducted. Correlations between scan path parameters and recognition of happy facial expressions could not be performed, as both groups performed at ceiling on these items. As earlier analyses indicated that the NF1 group spent less time viewing the face as a whole compared with TD controls, "MDTP to whole face" was included in the correlational analyses. All correlations are displayed in Table 3.

Table 3

Correlations between scan path parameters, age-adjusted Facial Recognition Test scores, and social competence ratings in the NF1 group.

	Emotion recognition (percent correct)			
	Total	*Neutral*	*Angry*	*Fearful*
Face Scan Paths				
MDTP to eye region	.167	-.006	.092	.223
MDTP to nose	-.175	-.358	-.071	-.101
MDTP to mouth	-.093	-.019	.038	-.152
MDTP to non-feature facial regions	.113	.230	-.057	.162
MDTP to whole face	.197	-.083	.157	.276
Face Perception and Social Competence				
Facial Recognition Test Z-score	.235	-.122	.364*	.040
Social Competence with Peers raw score	-.178	-.296	-.161	-.018

Note: * = marginally significant trend (p = .052). No other correlations approached statistical significance.

As can be seen from Table 3, correlations between emotion recognition scores and scan path parameters did not approach statistical significance (all, $p \geq .067$), suggesting that emotion recognition skills were not related to time spent viewing facial features in the NF1 group.

Are emotion recognition deficits in NF1 related to poor face perception?

Non-parametric correlational analyses (Spearman's rho correlations) were conducted to investigate the relationship between emotion recognition problems and face perception abilities in the NF1 group. Correlations are displayed in Table 3. Analyses revealed a trend whereby better recognition of anger was associated with better face perception skills (p = .052), however no other correlations approached statistical significance (all, $p \geq .221$).

Are emotion recognition problems and/or face perception deficits related to day to day social competence in NF1?

We compared the mean SCPQ–P ratings in the NF1 group with the published normative mean (M = 14.82, SD = 3.12; Spence, 1995) using the non-parametric One-Sample Wilcoxon Signed Ranks Test. Results revealed that the NF1 group displayed significantly lower social competence ratings than the normative population (M = 11.17, SD = 6.46, p = .033).

Non-parametric correlational analyses (Spearman's rho correlations) were conducted to investigate the relationship between emotion recognition problems and social competence in the NF1 group. Correlations were based on raw scores for the SCPQ–P, as there was no significant relationship between social competence and chronological age in the NF1 group (ρ = -.161, p = .463). All correlations are displayed in Table 3. No correlations approached statistical significance (all, $p \geq .170$), suggesting that emotion recognition problems were not related to social competence problems in our NF1 cohort.

We also examined the Spearman's rho correlation between age-adjusted Facial Recognition Test Z-scores and Social Competence with Peers Questionnaire ratings in the NF1 group. This correlation was not statistically significant (ρ = .268, p = .217), indicating

that face perception problems were not related to day to day social competence problems in children with NF1[11].

Discussion

The primary aims of this study were to investigate emotion recognition skills, visual scanning of emotional facial expressions and face perception abilities in children with NF1 compared to their typically developing peers. Relationships between these skills were also explored. As predicted (Hypothesis 1), children with NF1 displayed significantly poorer facial emotion recognition skills than typically developing children. Specifically, children with NF1 displayed significant deficits in recognising fear, but not neutral or happy expressions. A trend was also observed whereby children with NF1 displayed poorer recognition of angry faces compared to TD controls, although this effect failed to reach statistical significance. These findings are at least partially consistent with those of previous studies in children and adults with NF1 (Huijbregts et al., 2010; Pride et al., 2014) and provide further empirical evidence to suggest that NF1 is associated with specific deficits in recognising negative emotions.

Our hypothesis that children with NF1 would display aberrant face scan paths (Hypothesis 2) was partially supported. Contrary to predictions, children with NF1 did not spend less time viewing individual core facial features (eye region, nose, mouth, and non-feature regions) compared to TD controls. Nevertheless, there was a significant difference between children with NF1 and TD controls in time spent viewing the face as a whole (i.e. a greater percentage of time spent viewing background/off-image screen areas), suggesting that children with NF1 spend less time than is typical looking at faces, at least when they are presented in isolation.

[11] To investigate the relationship between social competence and face perception in the NF1 group further, we split the NF1 group into two subgroups based on FRT performance – "impaired" (Z-score ≤ -1.5) and "intact" (Z-score > -1.5) – and compared social competence ratings between the subgroups using independent samples t-test. Results were not statistically significant (p = .330).

In line with our prediction (Hypothesis 3), on average, children with NF1 displayed significantly poorer face perception abilities than controls. Indeed, 24% of our NF1 sample performed within the clinically impaired range on our face perception task. These findings are consistent with those of Huijbregts et al. (2010), who reported deficits in facial recognition accuracy and response speed in their NF1 sample and provide support for the notion that face perception problems may be an important aspect of the neuropsychological phenotype of children with NF1. The present study extends the findings of Huijbregts et al. (2010) by providing additional information as to the specific nature of the facial recognition deficits documented in NF1. Specifically, while the facial recognition task employed by Huijbregts et al. (2010) involved both visual working memory and face perception components, the self-paced Facial Recognition Test employed in the present study was a 'pure' perceptual discrimination/matching task. Thus, the present findings indicate that children with NF1 have significant difficulty processing face stimuli at the basic visuoperceptual level. These findings suggest a need to incorporate screening for face perception problems into more general clinical assessment protocols for children with NF1, as previous research has indicated that face perception difficulties may impact negatively on the development of self-esteem, emotional wellbeing and social relationships, at least in children with developmental prosopagnosia (Yardley, McDermott, Pisarski, Duchaine, & Nakayama, 2008).

Our hypothesis that emotion recognition deficits would be related to less time spent viewing core facial features in children with NF1 (Hypothesis 4) was not supported. However, there was partial support for our hypothesis that emotion recognition deficits would be related to poor face perception in children with NF1 (Hypothesis 5), as there was a marginally significant trend whereby poorer recognition of angry facial expressions in children with NF1 was associated with poorer face perception performance. A similar trend has been reported whereby larger grey matter volume in the left fusiform gyrus – an area

associated with human face detection (Grill-Spector et al., 2004) – was associated with poorer emotion recognition in adults with NF1 (Pride et al., 2014). Our results suggest that face perception problems may, at least partially, contribute to the social perceptual difficulties observed in NF1.

Contrary to predictions (Hypothesis 6), our present findings failed to indicate a significant relationship between emotion recognition or face perception skills and social competence in children with NF1, at least based on parent-rated questionnaires of day to day social competence.

Limitations and Future Directions

There were several methodological limitations in the present study which must be considered. Firstly, although an NF1 sample of 29 children is reasonable relative to other studies in the area (e.g. Huijbregts et al., 2010; Huijbregts & De Sonneville, 2011), a larger sample size would allow for a more comprehensive exploration of the influence of other potential mediating variables on social information processing and visual scanning behaviour in this population, including chronological age and psychological comorbidities.

The demographic differences between our NF1 and TD control groups must also be considered. Although the two groups did not differ significantly from one another in terms of gender distribution, there was a trend towards a higher distribution of females in the NF1 sample than in the TD control group. As females in the NF1 and TD control groups displayed significantly better emotion recognition accuracy than males in our study, it is assumed that the gender imbalance did not significantly influence the observed pattern of results – that is, we would expect any existing group differences in emotion recognition to be reduced rather than increased as a function of gender. Nevertheless, future studies should aim to match participants on both age and gender to rule out this potential source of bias.

In the present study, we failed to detect any significant relationships between emotion recognition, face perception and daily social competence in children with NF1. Notably, however, our study solely relied on a parent report measure of social competence, which may be less sensitive than teacher report or peer report measures or direct observation. Future research in this area should supplement parent reports of social competence with additional sources of information.

Another potential limitation of the present study was the passive gaze recording method that we employed. While similar methods have been employed in previous studies investigating scan paths and emotion recognition in other neurodevelopmental disorders (e.g. Pelphrey et al., 2002; Shaw & Porter, 2013) and while we deliberately chose this method in light of research demonstrating that the addition of a cognitive task can significantly impact visual scanning behaviour (Hayhoe & Ballard, 2005; Land, 2009), it could be argued that concurrent emotion recognition and visual scan path recording would provide more useful clinical information as to how children with NF1 extract and interpret information from facial expressions of emotion. Future research in this area would benefit from concurrent emotion recognition and visual scan path recording, to examine whether the addition of an explicit emotion recognition task influences face scanning behaviour in children with NF1, especially since we did not find less time spent viewing core facial features in our clinical sample.

Our finding that children with NF1 spent less time viewing the face as a whole compared to TD controls warrants further exploration. Notably, time spent viewing the face as a whole was not significantly related to parent ratings of ADHD symptomatology in our sample of children with NF1, suggesting that comorbid ADHD did not contribute significantly to the aberrant face scan paths observed in our clinical sample. This being said, the relationship between ADHD and face scanning behaviour in children with NF1 merits further study, particularly in light of previous research suggesting impaired facial emotion

recognition skills and aberrant face scan paths in children with ADHD only (Marsh, 2008). Future research should aim to recruit a large number of children with NF1 with and without comorbid ADHD diagnoses, as well as an ADHD only comparison group, to compare face scan paths between these groups and examine whether the presence of comorbid ADHD influences visual face scanning behaviour (particularly, time spent looking outside the face) in those with NF1. Future research in this area should also aim to incorporate control stimuli (e.g. images of inanimate objects) to determine whether this visual scanning behaviour is specific to faces in this cohort. It would also be interesting to use eye-tracking methods to examine attention to faces in children with NF1 when there is additional competing non-social information – for example, in the context of a natural scene, which would provide a more ecologically valid measure of social processing.

Identifying the factors contributing to emotion recognition deficits in individuals NF1 is an important challenge for future research, as this information will assist clinicians working with these individuals in designing appropriate intervention and remediation programs. While the present pattern of results suggests that face perception problems may contribute to poor emotion recognition in NF1, face perception problems are certainly not sufficient to account entirely for these observed emotion recognition deficits. Furthermore, emotion recognition deficits in NF1 do not appear to be significantly related to face scan paths in this cohort. The nature of the emotion recognition problems documented in NF1 – that is, specific difficulty in recognising negative emotions such as fear and, to a lesser extent, anger – may suggest a potential role for amygdala dysfunction in this population. Notably, amygdala dysfunction has been documented in other neurodevelopmental and anxiety disorders characterised by impaired recognition of negative emotions, including autism spectrum disorder (Pelphrey, Adolphs, & Morris, 2005; Schultz, 2005) and social anxiety disorder (Sladky et al., 2015). Furthermore, recent evidence suggests that individuals with NF1 show abnormal functional

connectivity between the orbitofrontal cortex and the amygdala, which is significantly associated with deficits in aspects of social, behavioural and cognitive functioning (Loitfelder et al., 2015). Future research employing concurrent emotion recognition tasks, eye-tracking and neuroimaging in children and adults with NF1 would be informative to explore the relationships between emotion recognition skills and neural activation in these individuals.

Conclusion

The present study suggests that children with NF1 display face processing abnormalities and specific deficits in recognising negative emotional expressions, especially fear. Nevertheless, the factors contributing to face perception and emotion recognition problems in NF1 remain unclear and warrant further investigation. Taken together, our findings suggest that impairments in the perception, identification and interpretation of information from faces are important aspects of the social-cognitive phenotype of NF1. Our findings highlight a need to incorporate screening for face perception and emotion recognition problems into the general clinical management of individuals with NF1.

Author Contributions

This study was conceived by Melanie Porter, Jonathan Payne, Kathryn North, Tracey Williams and Samantha Bzishvili. Amelia Lewis took the leading role in collecting and analysing data (with the assistance of Ms Bzishvili) and drafting the manuscript. Melanie Porter, Jonathan Payne and Tracey Williams assisted with data interpretation and revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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PAPER 3

How Children with Neurofibromatosis Type 1 Process Faces within a Social Scene

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Abstract

This study employed eye-tracking technology to investigate attention to faces within a social scene in 24 children with neurofibromatosis type 1 (NF1) compared to 24 typically developing controls matched for chronological age and handedness. The relationships between time taken to first fixate on a face within a scene, total time spent viewing faces within a scene and face perception abilities were also explored. Results indicated that children with NF1 did not take longer than controls to first fixate on a face within a scene, however children with NF1 spent significantly less time overall viewing faces within social scenes compared to controls. Children with NF1 also displayed significantly poorer face perception abilities than controls. Correlational analyses did not reveal any significant relationships between face perception abilities, time to first fixation on faces or time spent viewing faces within social scenes. These findings contribute to a growing body of literature suggesting that abnormal face processing is a key aspect of the social-cognitive phenotype of NF1.

Key Words: NF1, attention, face processing, face perception, social scenes.

Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder associated with reduced social skills (Barton & North, 2004; Noll et al., 2007; Pride, Crawford, Payne, & North, 2013) and specific cognitive deficits, particularly in the domains of attention, visuospatial skills, language, and executive function (Hyman et al., 2005; Lehtonen, Howie, Tump, & Huson, 2013; Payne, Hyman, Shores, & North, 2011; Rowbotham, Pit-ten Cate, Sonuga-Barke, & Huijbregts, 2009). Although intellectual functioning falls broadly within the normal range, a downward shift in overall intelligence levels is evident when compared with the general population (Feldmann, Denecke, Grenzebach, Schuierer, & Weglage, 2003; Ferner, Hughes, & Weinman, 1996; Hyman et al., 2005). Given their significant social and cognitive difficulties, there has been recent interest in better understanding how individuals with NF1 process social information, including faces. To this end, studies have identified deficits in both face perception (the ability to discriminate between and match physical characteristics of faces) and facial emotion recognition in adults and children with the condition (Huijbregts, Jahja, De Sonneville, De Breij, & Swaab-Barneveld, 2010; Lewis, Porter, Payne, Williams, & Bzishvili, in prep; Pride et al., 2014). Taken together, these findings suggest that aberrant face processing may be an important feature of the social phenotype of NF1. Nevertheless, no studies to date have investigated whether individuals with NF1 display reduced attention to faces in a naturalistic setting – for example, within the context of a social scene. The aim of the present study, then, was to employ eye-tracking technology to investigate whether children with NF1 differ from typically developing children in the way they attend to faces within a social scene.

Face Processing in NF1

Three studies have investigated the manner in which individuals with NF1 process information from faces. Huijbregts et al. (2010) investigated face processing skills in children

and adolescents with NF1 using computerised tests from the Amsterdam Neuropsychological Tasks battery (De Sonneville, 1999). Significant deficits in both facial emotion recognition skills and facial recognition skills in their NF1 sample compared to healthy controls were reported. Specifically, children and adolescents with NF1 were less accurate than controls in their ability to identify and match photographs of fearful and angry facial expressions. The NF1 group was also slower and less accurate than the control group at recognising whether or not photographs of neutral target faces appeared in a subsequent set of four response photographs. As the target and response stimuli in the facial recognition task employed by Huijbregts et al. (2010) were not presented simultaneously, it is difficult to interpret whether the deficit observed in the NF1 group reflected specific face perception problems or more general difficulties with visual working memory, a cognitive domain previously documented as impaired in children and adolescents with NF1 (Rowbotham et al., 2009). Nevertheless, this study provided the first empirical evidence to suggest the presence of face processing abnormalities in NF1. Subsequent studies have also suggested face processing impairments in this population (e.g. Pride et al., 2014).

Pride et al. (2014) reported that adults with NF1 displayed significantly poorer accuracy than typically developing controls on a task which required them to identify the emotions portrayed by actors in brief video vignettes using facial expressions, intonation and gestural cues. A particular deficit was evident in their cohort for recognition of anger. The authors also used volumetric neuroimaging techniques to investigate neural correlates of emotion recognition problems in participants with NF1 and reported a non-significant trend whereby larger grey matter volume in the left fusiform gyrus was associated with poorer overall emotion recognition in their NF1 sample. As the fusiform gyrus has been shown to be involved in the detection and identification of human faces (Grill-Spector, Knouf, &

Kanwisher, 2004), the authors proposed that aberrant face processing may contribute, at least to some extent, to the emotion recognition problems observed in people with NF1.

In keeping with Huijbregts et al. (2010) and Pride et al. (2014), Lewis et al. (in prep) also reported significant deficits in facial emotion recognition and face perception skills in children with NF1. Specifically, on a forced-choice emotion recognition task, children with NF1 demonstrated significant impairments compared to typically developing controls in their ability to identify photographs of facial expressions of fear, but not neutral or happy expressions. A non-significant trend was also observed whereby children with NF1 displayed poorer recognition of anger than controls. Children with NF1 also displayed significant impairments in their ability to match and discriminate between photographs of unfamiliar faces using the standardised Facial Recognition Test (Benton, Sivan, Hamsher, Varney, & Spreen, 1994), suggesting a significant deficit in face perception in this cohort. Correlational analyses failed to detect any significant relationships between facial emotion recognition skills and face perception skills in the NF1 group, nevertheless a trend was observed whereby NF1 children with more impaired face perception skills demonstrated significantly poorer recognition of angry facial expressions. Taken together, these findings provide some empirical evidence to support the presence of face processing abnormalities in individuals with NF1.

Measuring Attention to Faces: A Role for Eye-Tracking Technology

The development of eye-tracking technology has provided researchers with a useful means of exploring the manner in which attention, as measured by eye-gaze, is allocated to different classes of visual stimuli. While the authors acknowledge that eye-gaze is not completely analogous with attention, there is increasing research within the neurodevelopmental literature suggesting that scan path analysis allows researchers to map the spatiotemporal location(s) of focussed attention (Noton & Stark, 1971) and so develop a

better understanding of how individuals analyse and perceive visual material (e.g. see Williams, Porter, & Langdon, 2013; Wilson, Brock, & Palermo, 2010). Of note, only one study to date has used eye-tracking technology to investigate face processing in children with NF1. Lewis et al. (in prep) analysed the face scan paths of children with NF1 aged between 6 and 13 years and found that they did not differ significantly from typically developing controls in the percentage of time they spent attending to the eyes, nose, mouth, and non-feature facial regions of faces. Nevertheless, children with NF1 spent significantly less time viewing internal facial features overall when compared to typically developing controls. These findings suggest that children with NF1 differ from typically developing children in the degree of visual attention they allocate to faces, at least when presented in isolation. However, it is not clear whether children with NF1 spend less time than is typical attending to faces in a more naturalistic setting.

While studying attention to faces presented in isolation may yield valuable information, important aspects of genuine social interactions are absent from these stimuli (Risko, Laidlaw, Freeth, Foulsham, & Kingstone, 2012). Complex social scenes containing both social and non-social information represent a particularly useful class of stimuli for eye-tracking studies as they allow investigation of attention to faces in a more ecologically valid manner. While no studies to date have examined social scene processing in individuals with NF1, reduced attention to faces and/or people in social scenes has been documented in other neurodevelopmental disorders characterised by impaired social processing, including autism spectrum disorder (e.g. see Riby & Hancock, 2008; Wilson et al., 2010) and Fragile X syndrome (e.g. see Williams et al., 2013). For example, both Riby and Hancock (2008) and Wilson et al. (2010) reported that children with autism spectrum disorder spent less time overall viewing faces in static social scenes compared to typically developing controls. Riby and Hancock (2009) also replicated this finding in children with autism spectrum disorder

using dynamic social stimuli in the form of movie and cartoon clips. Similarly, Williams et al. (2013) found that children with Fragile X syndrome were significantly slower than controls to orient their attention towards social information (faces and people) presented non-centrally within a social scene, although total time spent viewing social stimuli did not differ significantly between the Fragile X and control groups. It will be important to investigate whether children with NF1 display aberrant scene-processing patterns, particularly in light of the growing body of evidence suggesting impaired processing of social information (and especially faces) in children with NF1.

Attention to Faces and Face Perception Skills

Literature on the development of face recognition skills suggests an integral relationship between face perception and attention to faces in the natural environment. Leading theories on the development of face perception skills suggest that infants may display an innate attentional bias towards faces in their environment, which is hypothesised to occur via a specific subcortical mechanism (Morton & Johnson, 1991). This attentional bias would result in repeated exposure to faces during infancy and, through this process, brain tissue in the inferotemporal cortex is argued to become specialised for face detection (Nelson, 2001). As such, individuals who do not display an attentional preference for faces during early development may well fail to acquire normal face perception abilities and normal face processing networks, as is hypothesised to occur in children with autism spectrum disorder (Grelotti, Gauthier, & Schultz, 2002). An alternative explanation proposed by Wilson et al. (2010) is that an individual's face perception skills might impact on the manner in which they allocate attention to aspects of their environment, such that children with face perception problems may gain less information from social stimuli, thereby developing an attentional bias towards non-social information. Regardless of the direction of causality, theoretical

foundations suggest a relationship between the development of face perception skills and attention to faces in the environment.

There is a growing body of empirical evidence to suggest the presence of face perception problems in individuals with NF1 (Huijbregts et al., 2010; Lewis et al., in prep; Pride et al., 2014). The findings of Lewis et al. (in prep) further suggest that children with NF1 spend less time viewing faces presented in isolation than typically developing children. Of note, significant associations between face perception problems and reduced attention to social stimuli have been identified in other developmental disorders, most notably autism spectrum disorder (e.g. Grelotti, Gauthier, & Schultz, 2002; Wilson et al., 2010). For example, Wilson et al. (2010) investigated the relationships between attention to people within a social scene (that is, total time viewing people and preference for initially fixating on people versus objects within the scene) and face-matching abilities in children with ASD. While they failed to detect a significant relationship between face-matching performance and total time spent looking at people in their ASD sample, a significant correlation was revealed whereby children with poorer face-matching skills showed a significant initial preference for fixating on objects relative to people within the scenes. No study to date has investigated the relationship between face perception abilities and attention to faces in NF1.

Aims of the Present Study

The primary aim of the present study was to use eye-tracking technology to investigate attention (as measured by eye-gaze) to faces in children with NF1 within a semi-naturalistic setting – that is, in the context of a static social scene. More specifically, the study aimed to investigate whether or not children with NF1 take longer to first fixate on a face and/or spend less time overall looking at faces within a scene than typically developing children, as has been shown in other neurodevelopmental disorders characterised by impaired social information processing. Since face perception deficits have been documented in

children with NF1 (Huijbregts et al., 2010; Lewis et al., in prep), we also examined the relationship between attention to faces and face perception abilities in this cohort. In keeping with the face processing literature from other neurodevelopmental disorders, it was hypothesised that children with NF1 would take longer to first fixate on face stimuli (Hypothesis 1a) and spend less time overall viewing faces (Hypothesis 1b) within social scenes compared to typically developing age-matched controls. It was also predicted that poorer face recognition skills in children with NF1 would be associated with longer time to first fixation to faces (Hypothesis 2a) and smaller percentage of time spent looking at faces within a scene (Hypothesis 2b).

Method

Participants

Participants were 24 individuals with NF1 and 24 typically developing (TD) controls[12], matched individually for chronological age (within 6 months) and matched at the group level on handedness. All participants displayed normal or corrected to normal vision.

NF1 participants in this study were recruited through the Neurogenetics Clinic at The Children's Hospital at Westmead (CHW), Sydney, Australia. This clinic caters for over 1300 individuals with NF1 and has a wide referral base, with all socioeconomic groups represented. Children were recruited if they met the following inclusion criteria: (a) confirmed diagnosis of NF1 based on criteria specified by the National Institutes of Health Consensus Conference (NIH, 1988), (b) absence of diagnosed intracranial pathology (e.g. epilepsy, traumatic brain injury, or brain tumour), (c) an IQ $\geq$ 70, (d) no current or previous diagnosis of anxiety disorder, mood disorder, or psychotic disorder, and (e) competency in the English language. One NF1 participant was excluded due to failure to meet criterion (c). A review of clinical records revealed that five NF1 participants had a diagnosis of Attention Deficit Hyperactivity

[12] 25 NF1 participants were originally recruited however one had to be excluded (see criteria below).

Disorder (ADHD), however we decided to include these participants in our study in order to provide the most representative sample of children with NF1 in light of the high rates of comorbid ADHD reported in this population (Hofman, Harris, Bryan, & Denckla, 1994; Mautner, Kluwe, Thakker, & Leark, 2002). Approval for the study was granted by the Children's Hospital at Westmead and Macquarie University Human Research Ethics Committees. Written informed consent was obtained from all participants' parents.

Typically developing (TD) controls were recruited through Neuronauts, a kids' research participation club at Macquarie University, Sydney, Australia. Exclusion criteria were a history of developmental delay, significant sensory impairments (that would impact on normal development and on their ability to complete the research tasks), intellectual or other cognitive impairments, neurological disorders, psychological or psychiatric disorders, or English as a second language. No children were excluded based on these criteria.

Table 1 displays the demographic characteristics of each group. As shown in Table 1, chi-square analysis revealed no significant difference in sex distribution between the groups, although a non-significant trend was observed whereby there was a somewhat higher proportion of female participants in the NF1 group. Chi-square test also confirmed no group difference in handedness. Independent samples *t*-test confirmed that the two groups were well matched in terms of chronological age.

Table 1

Demographic characteristics for each group.

	NF1 group ***Mean (SD)*** *Range*	TD group ***Mean (SD)*** *Range*	*t* score	*p* value
Males : Females	7 : 17	13 : 11	3.086ˆ	.079
Right-Handed : Left-Handed	22 : 2	22 : 2	.000ˆ	1.000
Chronological Age (years)	**10.37 (1.80)** 6.67 – 12.92	**10.34 (2.02)** 6.67 – 13.42	.050	.961

ˆ Chi-square statistic

Materials

Social Scene Stimuli

Stimuli included 18 images of social scenes taken from the International Affective Picture System (IAPS; Lang et al., 1999). The IAPS is a set of photographs depicting various stimuli, including animals, social scenes and landscapes that is widely used in studies of emotion, arousal, and visual tracking (Mikels et al., 2005). Each image used in the current study contained at least one person in a natural scene, with at least one face visible (IAPS images used in this study included IDs: 2235, 2272, 2299, 2393, 2396, 2398, 2480, 2514, 2560, 2575, 2579, 2590, 2593, 2594, 2598, 2749, 5875 and 7550).

Facial Recognition Test – Long Form

The Facial Recognition Test (Benton et al., 1994) is a self-paced neuropsychological measure of face perception skills which assesses the examinee's ability to match and discriminate between photographs of unfamiliar human faces. The test is made up of 54 response items requiring the examinee to match front-view photographs of faces with identical front-view faces, three quarter faces, and faces under different lighting conditions. In the present study, raw scores were converted into age-adjusted Z-scores based on normative data reported by Paquier et al. (1999)[13]. The Facial Recognition Test has a reported internal consistency reliability coefficient of 0.71 in a sample of older adults (Christensen, Riley, Heffernan, Love, & McLaughlin Sta. Maria, 2002). Psychometric properties of the test are considered acceptable, but fall below levels recommended for diagnostic use (Strauss, Sherman, & Spreen, 2006),

[13] Paquier et al. (1999) published Facial Recognition Test norms for typically developing children aged between 7 and 14 years. Z-scores were generated based on 7-year-old age norms for the two 6-year-old participants in the present study (one NF1 participant and one TD participant).

Procedure

Participants viewed the images on a Dell 16" FP monitor in a darkened room. Scenes were presented in the centre of the computer screen at a standardized size of 25.14cm (950 pixels) x 18.84cm (712 pixels), width by height. The eye-tracking task was completed in a single testing session along with intelligence screening measures and the Facial Recognition Test.

Eye-Tracking Procedure

Participants' eye movements were recorded using an Eyelink 1000 (SR-Research Ltd.) remote eye-tracking camera at a sampling rate of 500 Hz. For most participants, calibration, validation, and scan path recordings were made for the right eye. Calibration for the right eye was unsuccessful for two participants in the NF1 group, so the calibration procedure was repeated for the left eye and subsequent eye movement recordings were made for the left eye.

A nine point calibration method was used to calibrate and validate participants' eye movements prior to the social scene trials. Participants were instructed to fixate on a centrally placed black dot (10mm in diameter) which appeared in the centre of the screen. The dot then moved to eight different locations around the periphery and centre of the screen, and participants were instructed to follow its movements with their eyes. The dot moved to a new location when participants had fixated on the dot for at least 1000 ms. The experimental procedure only proceeded once a satisfactory calibration was achieved, ensuring that a robust and accurate fixation recording could be obtained at any point on the computer screen.

A black dot was presented in the centre of the screen for 1000 ms immediately prior to each social scene to control for the initial point of retinal attention. Participants were only able to progress to the next social scene trial once they had fixated continuously on this central dot for 2000 ms. Once an adequate central fixation was recorded, manual experimenter control initiated the next trial, and the central fixation dot disappeared and was replaced by a social

scene. This ensured that all participants were attending to the centre of the screen as soon as the image appeared. Central fixation re-appeared in between each social scene trial.

In order to record the most naturalistic scan path information, participants were instructed only to "look at" each image. Scene stimuli were viewed passively for 10,000 ms each. The 10,000 ms exposure time was selected to ensure that there was sufficient time to investigate scan path patterns for all parameters, as in previous research (e.g. Williams et al., 2013).

Areas of Interest

Areas of interest were traced using the Eyelink Data Viewer freehand drawing function. For all scenes, a 'Faces' area of interest was defined as the sum of all faces (traced around the hairline) within the scene.

Visual Scan Path Parameters

Visual scan path parameters selected for analysis included: Mean Time to First Fixation (mean length of time in milliseconds for the first fixation to enter a defined area of interest[14]), Mean Dwell Time Percent (mean percentage of time spent attending to an area of interest relative to the total time spent attending to the screen) and Mean Fixation Percent (mean percentage of fixations made within a defined area of interest). Similar patterns of results were found for Mean Dwell Time Percent and Mean Fixation Percent, and so only the former is reported here. A Proportional Mean Dwell Time Percent to Faces was then generated, defined as Mean Dwell Time Percent to Faces divided by the Mean Dwell Time Percent to the whole scene image. The Proportional Mean Dwell Time Percent was used for analyses investigating Hypothesis 1b (that children with NF1 would spend less time overall viewing faces than controls) in order to ensure that the experimental results reflected 'true'

[14] If no fixations were made to the eye region during an experimental trial, the maximum time until first fixation (10,000ms) was entered for that trial. Similar methods have been employed in previous studies (e.g. Wilson et al., 2010).

attention to face stimuli in the context of the social scenes rather than 'off-task' behaviour (e.g. eye movements directed outside the image). This was considered to be particularly important given the high rates of comorbid ADHD observed in the NF1 group.

Statistical Analysis

Data were analysed using Predictive Analytics SoftWare (PASW) Statistics Version 18 for Windows. A *p* value of 0.05 was used for all analyses to indicate statistical significance.

Results

Do children with NF1 take longer to initially look at faces within a scene?

Figure 1 displays the Mean Time to First Fixation to Face stimuli in milliseconds (averaged across all social scenes) for the NF1 and TD control groups. Independent samples *t*-test revealed that there was no significant difference between the groups in the amount of time taken to initially fixate on faces within a scene ($t_{(46)} = .50$, $p = .617$, $r = 0.07$), suggesting that children with NF1 did not initially avoid looking at faces within a scene compared to TD controls.

Given the uneven male:female ratio in the present study, Pearson product-moment correlations between gender and Mean Time to First Fixation to Face stimuli were examined for the NF1 and TD control groups to address the possibility of bias due to gender effects. There were no significant relationships between these variables in the NF1 or TD control groups (both, $p \geq .821$).

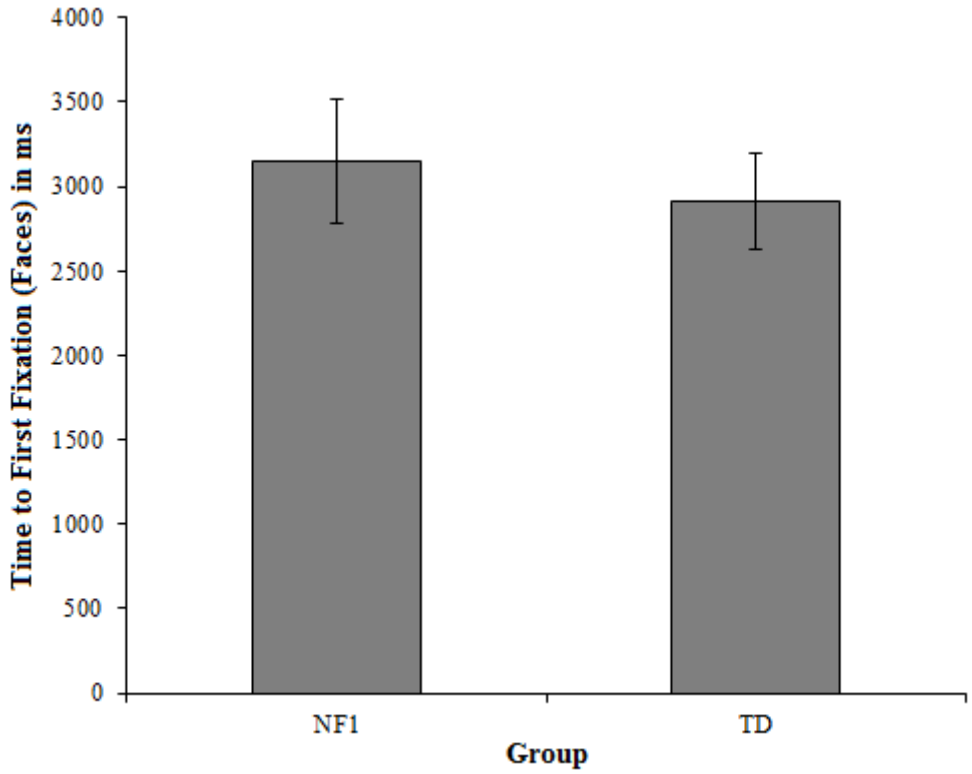

Figure 1. Mean Time to First Fixation to Face stimuli for NF1 and TD control groups. Error bars represent +/- 1 standard error.

Do children with NF1 spend less time viewing faces within a scene?

Figure 2 displays the Proportional Mean Dwell Time Percent to Faces (averaged across all social scenes) for the NF1 and TD control groups. Independent samples *t*-test revealed a significant difference between the groups, such that, on average, the NF1 group spent less time attending to faces in the scenes compared to TD controls ($t_{(46)}$ = -2.03, p = .048, r = 0.29).

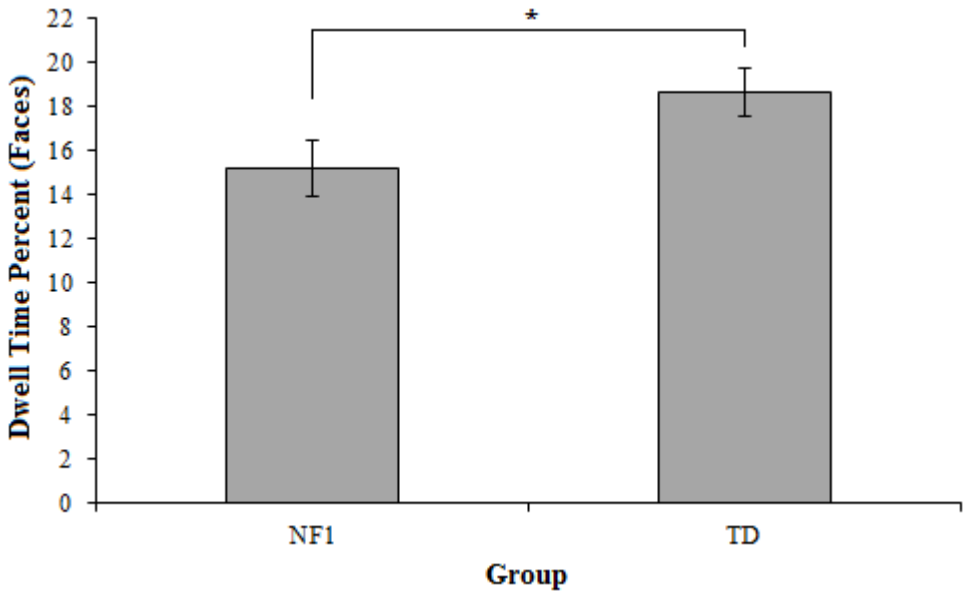

Figure 2. Proportional Mean Dwell Time Percent to Faces for NF1 and TD control groups. Error bars represent +/- 1 standard error. * = $p < .05$.

To address the possibility of bias due to gender effects, Pearson product-moment correlations between gender and Proportional Mean Dwell Time Percent to Faces were examined for the NF1 and TD control groups. There were no significant relationships between these variables in the NF1 or TD control groups (both, $p \geq .343$).

Do children with NF1 demonstrate face perception deficits?

Table 2 displays the mean age-adjusted Z-scores on the Facial Recognition Test in the NF1 and TD groups. Independent samples *t*-test revealed a significant difference between the groups, such that the NF1 group displayed significantly lower face perception abilities than the TD group ($p = .001$, $r = 0.46$). Four children in the NF1 group (16.67%) fell within the impaired range on the Facial Recognition Test (Z-scores ≤ -1.5), while no controls performed within this range.

Table 2

Mean Z-scores on the Facial Recognition Test in the NF1 and TD groups.

	NF1 group ***Mean (SD)*** *Range*	TD group ***Mean (SD)*** *Range*	*t* score	*p* value
Facial Recognition Test (Z-score)	**-0.56 (1.03)** -2.90 – 2.33	**0.50 (1.05)** -1.41 – 2.67	-3.562	.001*

* = statistically significant difference ($p < .05$)

To address the possibility of bias due to gender effects on Facial Recognition Test performance, Pearson product-moment correlations between these variables were examined for the NF1 and TD control groups. There were no significant relationships between gender and Facial Recognition Test performance in the NF1 or TD control groups (both, $p \geq .129$).

Is the amount of time taken to initially fixate on faces within a social scene related to face perception skills in children with NF1?

The Pearson product-moment correlation between Facial Recognition Test Z-score and Mean Time to First Fixation to Faces was examined in NF1 participants to investigate the relationship between face perception skills and time taken to initially fixate on faces in the NF1 group. There was no significant relationship between Facial Recognition Test performance and Mean Time to First Fixation to Face stimuli in the NF1 group ($r = .247$, $p = .245$) or the TD group ($r = -.003$, $p = .990$).

To investigate further the relationship between face perception and Mean Time to First Fixation to Faces, we generated a dot plot displaying the distribution of Mean Time to First Fixation to Faces for participants in the NF1 group who performed within the impaired and intact ranges on the Facial Recognition Test. These data are displayed in Figure 3 and demonstrate that those NF1 children with impaired face perception did not take longer than the rest of the NF1 group to initially fixate on faces within the scenes.

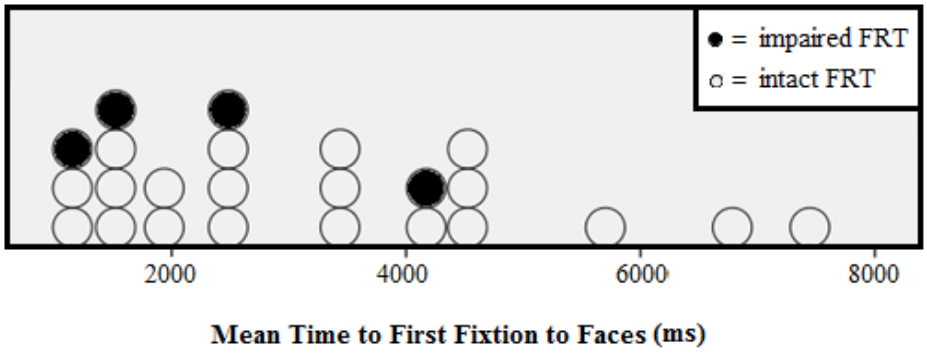

Figure 3. Dot plot showing Mean Time to First Fixation to Faces for participants with impaired and intact face perception.

Is the amount of time spent viewing faces within a social scene related to face perception skills in children with NF1?

To investigate the relationship between face perception skills and time spent attending to faces in the NF1 group, the Pearson product-moment correlation between Facial Recognition Test Z-score and Proportional Mean Dwell Time Percent to Faces was examined. There was no significant relationship between Facial Recognition Test performance and Proportional Mean Dwell Time Percent to Faces in the NF1 group (r = -.216, p = .311) or the TD group (r = .263, p = .215).

To investigate further the relationship between face perception and Mean Dwell Time Percent to Faces, we again generated a dot plot displaying the distribution of Mean Dwell Time Percent to Faces for participants in the NF1 group who performed within the impaired and intact ranges on the Facial Recognition Test. These data are displayed in Figure 4 and demonstrate that those NF1 children with impaired face perception did not spend less time looking at faces within the scenes.

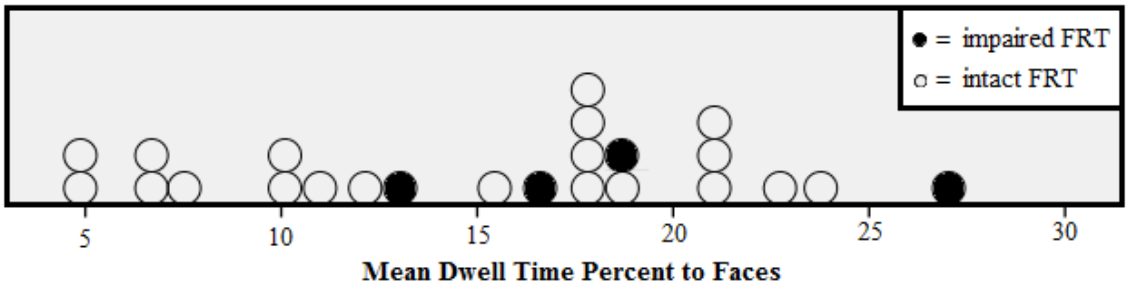

Figure 4. Dot plot showing Mean Dwell Time Percent to Faces for participants with impaired and intact face perception.

Discussion

The aims of this study were twofold: (1) to investigate the manner in which children with NF1 attend to faces within a social scene and (2) to investigate the relationship between attention to faces and face perception skills in these children. In relation to the first aim, contrary to our predictions, children with NF1 did not take longer than typically developing children to first fixate on a face within a social scene. This suggests that children with NF1 do not initially avoid looking at faces and are not less attracted to faces than controls. However, as predicted, children with NF1 spent significantly less time overall looking at faces within the scenes compared to controls. This is consistent with the limited available research in the area, which suggests that children with NF1 spend less time looking at faces than typically developing children when they are presented in isolation (Lewis et al., in prep). Nevertheless, this study extended previous findings by replicating this effect using more ecologically valid stimuli, which included both social and non-social information. Furthermore, in the present study we analysed the proportional mean dwell time percent which only took into account time spent attending to faces in the context of the entire scene. As such, our results reflect attention allocated to faces within social scenes rather than irrelevant off-task behaviour (e.g. time spent looking outside the image). These findings add to the growing body of research

supporting face processing abnormalities in individuals with NF1 (e.g. Huijbregts et al., 2010; Lewis et al., in prep; Pride et al., 2014).

In relation to the second aim, our hypothesis that attention to faces would be associated with face perception skills in children with NF1 (Hypothesis 2) was not supported. Although significant face perception deficits were evident in our sample of children with NF1 compared to controls, correlational analyses failed to detect a relationship between these skills and attention to faces within social scenes in our NF1 sample. Of note, these skills were also not significantly related in our typically developing sample. These findings are in part consistent with those of Wilson et al. (2010), who failed to detect a significant relationship between time spent viewing people and face perception skills in their sample of children with autism spectrum disorder, but identified a significant relationship between poorer face-matching skills and a preference for initially fixating on objects over faces in this group. We did not investigate relative attention to faces versus objects in our sample of children with NF1 in the present study, however this will be an important task for future research.

Limitations and Future Directions

The main limitation of the present study was our relatively small sample size. Although an NF1 sample of 24 children is reasonable in relation to other studies in this population (e.g. Huijbregts et al., 2010; Huijbregts & De Sonneville, 2011), a larger sample size would be beneficial for future studies, particularly so that individual differences in physical, cognitive and psychological disability and how these may relate to attention to faces in NF1 might be explored. In particular, future research should aim to recruit larger numbers of children with NF1 both with and without comorbid psychological diagnoses, as NF1 is associated with significantly higher rates of ADHD and autism spectrum disorder compared to the general population, as well as an increased risk of social anxiety disorder (Adviento et al., 2014; Garg et al., 2013; Hofman et al., 1994; Mautner et al., 2002; Pasini et al., 2012;

Walsh et al., 2013). As face processing abnormalities have been identified in individuals with ADHD, autism spectrum disorder and social anxiety disorder in the absence of NF1 (e.g. Chen, Ehlers, Clark, & Mansell, 2002; Marsh, 2008; Pelc, Kornreich, Foisy, & Dan, 2006; Riby & Hancock, 2008; Wilson et al., 2010), it will be important to consider the potential mediating effect of comorbid psychopathology on attention to faces in NF1.

Further study will be necessary to explore the mechanisms underlying the reduced attention to faces identified in children with NF1. In particular, it would be interesting to examine the influence of different task instructions on scene scanning behaviour in this cohort. While the present study investigated more naturalistic scanning of social scenes using only minimal task instructions (i.e. to "look at" each scene), the addition of an explicit social-cognitive task (e.g. "describe what is happening in this scene") may alter visual attention to faces in children with NF1. It would also be interesting to repeat our study using stimuli which more closely approximate real-world social interactions, such as dynamic social scenes (Risko et al., 2012). Although we failed to detect a relationship between face perception skills and attention to faces within static social scenes in our study, it would be important to re-examine the relationship between these skills in children with NF1 under these modified task conditions. It would also be interesting to explore whether there are particular regions of social scenes (e.g. other body parts, inanimate objects, background, etc.) at which children with NF1 are more likely to look, or whether the spatiotemporal scan paths of children with NF1 differ more generally from typically developing children. Unfortunately, the manner in which our areas of interest were defined precluded such an analysis here.

Investigating the relationship between attention to faces and day to day social functioning in children with NF1 will also be an important focus for future research. There is increasing evidence to suggest that NF1 is associated with both face processing abnormalities (e.g. Huijbregts et al., 2010; Lewis et al., in prep; Pride et al., 2014) and significantly poorer

social outcomes compared to the general population (e.g. Barton & North, 2004; Benjamin et al., 1993; Noll et al., 2007). However, the associations between these variables in children with NF1 remain unclear. Future studies should examine relationships between attention to faces in children with NF1 and parent, teacher, and self-report measures of day to day social function and psychological wellbeing. Developing a better understanding of how reduced attention to faces might impact on daily social functioning in children with NF1 would inform the development of social intervention and remediation programs at home and at school.

Implications

The extent to which reduced attention to faces might contribute to the social difficulties reported in NF1 has not been established. Our present findings suggest that clinicians and education professionals should consider the potential impact of both aberrant face perception and reduced attention to faces in children with NF1 when designing and implementing treatment programs for social dysfunction in this population. Faces are a unique class of visual stimuli, containing large amounts of socially relevant information, including another person's age, gender, thoughts and feelings and familiarity (Kanwisher & Moscovitch, 2000). As such, the ability to recognise, attend to and decode information from faces is critical for successful reciprocal social interactions. The present results suggest that children with NF1 may benefit from explicit instruction and practice aimed at teaching them how to attend to information from faces in their day-to-day social interactions. Designing and trialling intervention programs and examining their efficacy in children with NF1 will be important tasks for future researchers in the field of NF1.

Conclusion

Our findings suggest that children with NF1 spend less time attending to faces than typically developing children, at least when presented in the context of static social scenes. However, attention to faces does not appear to be related to face perception deficits in this

cohort. Exploring the mechanisms underlying this effect, as well as the relationships between reduced attention to faces and real-world social functioning in children with NF1 will be essential areas for future research.

Author Contributions

This study was conceived by Melanie Porter, Jonathan Payne, Kathryn North, Tracey Williams and Samantha Bzishvili. Amelia Lewis took the leading role in collecting and analysing data (with the assistance of Ms Bzishvili) and drafting the manuscript. Melanie Porter, Jonathan Payne and Tracey Williams assisted with data interpretation and revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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GENERAL DISCUSSION

This thesis was prompted by recent research suggesting impairments in socio-emotional functioning in children with NF1. The thesis had three aims in relation to children with NF1: 1) to investigate day to day social competence; 2) to better understand facial emotion recognition skills; and 3) to explore face processing and attention to faces. The following discussion summarises the main findings according to these three aims. Limitations, contributions to the literature, clinical and theoretical implications of this thesis and suggestions for future research are also highlighted below.

Day to Day Social Competence in Children with NF1

Paper 1 investigated day to day social competence in children with NF1 and the relationship between social competence and comorbid psychopathology (ADHD or ASD symptomatology), intellectual abilities and executive function. The first paper further established the existence of social competence problems in children with NF1 using a comprehensive measure addressing interpersonal relationships and perceived popularity. More specifically, the findings of Paper 1 indicated that children with NF1 display significantly poorer social competence than their typically developing peers, in line with previous research investigating social functioning in children with NF1 using the CBCL (e.g. Barton & North, 2004; Noll et al., 2007). Paper 1 extended existing findings by providing additional information as to the specific nature of the social competence problems in this population. That is, findings from this thesis showed that, on average, children with NF1 had greater difficulty forming and maintaining friendships, had poorer overall relationships with their classmates, were less popular than their peers and were less likely to see friends outside of school compared to typically developing children. However, they also displayed significantly greater individual variability in social competence compared to typically

developing children, with some children with NF1 falling in the 'normal' range and others demonstrating significant impairments in their social competence.

This study contributes further to the existing literature by providing information regarding the psychological mechanisms contributing to social competence problems in children with NF1. While children with NF1 and no comorbid psychopathology certainly displayed social competence problems, those children with NF1 and comorbid ASD symptomatology were most at risk of social competence impairments. In particular, autistic mannerisms (e.g. repetitive behaviours and a restricted range of interests), social communication difficulties and socially anxious behaviour were associated with significantly poorer social competence. In contrast, no significant relationships were identified between social competence and Full Scale IQ, executive function, or symptoms of ADHD in our NF1 cohort, suggesting that even children with relatively normal psychological and cognitive profiles might be at risk of social competence problems.

Overall, the results of Paper 1 suggest a need to incorporate assessment and intervention for social competence problems into the general clinical management of children with NF1, particularly those with high levels of ASD symptomatology and socially anxious behaviour.

Facial Emotion Recognition in Children with NF1

Paper 2 investigated facial emotion recognition in children with NF1. While the existence of specific emotion recognition problems has been previously documented in NF1 (Huijbregts, Jahja, De Sonneville, De Breij, Swaab-Barneveld, 2010), Paper 2 aimed to extend these findings by exploring whether or not facial emotion recognition skills were related to face scan paths and/or face perception abilities. Additionally, the relationship between facial emotion recognition and day to day social competence was investigated.

The results of Paper 2 were consistent with those of Huijbregts et al. (2010) and suggested that children with NF1 do indeed display impairments in recognising threatening facial expressions of fear and, to a lesser extent, anger, but not non-threatening (neutral and happy) facial expressions. Emotion recognition impairments were not significantly associated with face scan paths, face perception abilities or day to day social competence; however, a trend was observed whereby children with NF1 with poorer face perception abilities showed greater inaccuracies in identifying anger. This suggests that face perception problems may, at least partially, contribute to the social perceptual difficulties observed in NF1. This correlation may have failed to reach statistical significance due to a power issue in our relatively small sample of children with NF1 – an interpretation which would be supported by a retrospective power analysis we conducted based on the moderate correlation (r = .364) obtained. Future research in this area would be warranted to address this possibility.

Face Processing and Attention to Faces in Children with NF1

In addition to exploring facial emotion recognition skills, Paper 2 also explored face perception and face processing (visual scanning of faces) in children with NF1. No previous study had directly investigated face perception abilities or face scan paths in this population. This was considered particularly important in light of the emerging body of evidence suggesting specific social information processing impairments in children with NF1, which may be contributing to their observed social difficulties.

In terms of the percentage of time spent viewing core facial features, no significant differences were observed between children with NF1 and their typically developing peers. However, the results of Paper 2 suggested that, overall, children with NF1 spent less time viewing faces when presented in isolation than typically developing children, indicating reduced attention to faces in this population. Children with NF1 also displayed significantly poorer face perception abilities than controls. These findings provide preliminary evidence to

suggest that impairments in perceiving and attending to information from faces is part of the social-cognitive phenotype of NF1.

Paper 3 investigated attention to faces in children with NF1 further by examining attention to faces in the context of competing non-social information. Specifically, Paper 3 aimed to determine whether children with NF1 took longer to attend to faces and/or displayed reduced attention overall to faces compared to typically developing children in the more naturalistic context of a social scene. We were also interested in whether attention to faces was related to face perception abilities in children with NF1 in light of evidence suggesting a potential link between these skills in the typically developing population (e.g. see Morton & Johnson, 1991) and in children with autism spectrum disorder (Wilson, Brock, & Palermo, 2010).

The key finding from Paper 3 was that children with NF1 spent less time overall viewing faces in the context of a social scene compared to typically developing children, providing further evidence to suggest reduced attention to faces in this population. In contrast, our findings indicated that children with NF1 did not take longer than typically developing children to initially fixate on a face within a social scene. This would suggest that faces initially capture attention to the same extent in individuals with NF1 and in the typically developing population, but that children with NF1 do not continue to attend to faces for as long as their typically developing peers. Similar face scan path patterns have been documented in children with ASD (e.g. Riby & Hancock, 2008; Wilson et al., 2010) and are thought to reflect reduced social attention. As in Paper 2, face perception problems were identified in our sample of children with NF1. However, face perception abilities were not significantly related to time to first fixation or the percentage of time spent viewing faces in our clinical sample. Nevertheless, it would be interesting to investigate other scan path parameters relating to attention to faces (for example, the percentage of initial fixations made

to social versus non-social stimuli within a scene) to determine whether these might be related to face perception abilities in children with NF1. We were unable to conduct these analyses in the current thesis due to the manner in which areas of interest were defined for each social scene (i.e. data was only recorded for time to first fixation to each face, with all other stimuli included as 'background').

Taken together, the findings of Papers 2 and 3 suggest impairments in the perception, identification and interpretation of information from human faces in children with NF1.

Incidental Findings

While not specific aims or predictions of the present study, two incidental findings emerged in this thesis which contribute interesting and novel information to the literature on socio-emotional functioning in children with NF1. The first concerns the high rates of socially anxious behaviour that was observed in our sample of children with NF1. In Paper 1, we found that parent ratings on the Social Motivation subscale of the SRS (which taps into socially anxious and avoidant behaviours) were clinically elevated in 43.5% of our NF1 cohort. This is significantly elevated compared to the general population and would suggest a potential predisposition towards social anxiety disorder in children with NF1, although the SRS is only a screening measure and further diagnostic indicators of anxiety would be required before any firm conclusions could be drawn. Pasini et al. (2012) was the only study to previously examine anxiety symptomatology in children with NF1. In their study, the authors reported that children with NF1 displayed significantly higher total levels of anxiety symptomatology on a self-report measure compared to healthy controls, however they did not differ significantly from controls in their scores on disorder-specific subscales, including social anxiety. It is unclear why the rates of socially anxious behaviour were so high in our cohort. This may have reflected selection bias, with parents of children with NF1 with social anxiety more likely to volunteer their children for research addressing social functioning in

this population. Alternatively, the high rates of socially anxious behaviour in our cohort may indicate that the SRS is more sensitive than general anxiety screening measures in picking up symptoms of social anxiety in this population. Future research using a variety of anxiety screening measures, for example, the Spence Children's Anxiety Scale (Spence, 1997) or diagnostic interviews such as the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Kaufman et al., 2008), is certainly warranted to further explore socially anxious behaviour in children with NF1.

The relationships between social anxiety, social information processing and social competence certainly warrant further exploration in children with NF1. There is considerable evidence in the empirical literature that children with social anxiety disorders have poorer social outcomes than their non-anxious peers (Spence, Donovan, & Brechman-Toussaint, 1999; Strauss, Lease, Kazdin, Dulcan, & Last, 1989). There is also evidence to suggest that social anxiety is associated with an attentional bias away from emotional faces (Mansell, Clark, Ehlers, & Chen, 1999) as well as reduced time spent viewing the eye region of threatening faces as shown during eye-tracking tasks (Horley, Williams, Gonsalvez, & Gordon, 2003; Horley, Williams, Gonsalvez, & Gordon, 2004). It is possible that social anxiety is contributing to social information processing abnormalities and social competence problems in children with NF1 as children who are socially withdrawn may have less exposure to social stimuli and thus may be less efficient in attending to, encoding and interpreting social information. Future studies incorporating screening and diagnostic measures of anxiety symptomatology in children with NF1 could explore the potential mediating effect of social anxiety on social information processing and social competence in this population.

The second incidental, yet important, finding of this thesis concerns the extreme heterogeneity evident in children with NF1. Across all three papers of this thesis, considerable

individual differences were observed between participants across a number of neuropsychological domains including, but not limited to: social competence; psychological comorbidities; executive functioning; face perception abilities and attention to faces. Some children performed within the normal range on all measures, while others were significantly impaired in one or more neurocognitive domains. These findings are consistent with my own observations and interactions with children with NF1 throughout the testing process, with some children presenting as articulate, socially aware and engaged, while others had clear difficulty sustaining their attention and appeared reluctant to interact with others. The significant heterogeneity demonstrated in children with NF1 throughout this thesis has important clinical implications. Firstly, our findings highlight the need for comprehensive pre-screening measures to identify specific impairments which might impact on social functioning when working with this clinical group. Moreover, our findings suggest that a "one size fits all" approach to assessment and intervention and access to services for children with NF1 would be inappropriate.

Limitations

Study limitations have been identified and addressed in detail throughout Papers 1, 2 and 3 and will not be reiterated here. Of note here, however, the participants in Papers 1, 2 and 3 were all administered a large battery of tests addressing various aspects of social competence, psychopathology, cognitive functioning and social information processing. While every effort was made to obtain complete data sets for all participants, this was not always possible due to time constraints and/or technical difficulties on the day of testing. As such, certain relationships which we would have liked to explore in greater detail (for example, the relationship between social competence and attention to faces within the context of a social scene in our NF1 participants or the relationships between face scan paths and

Social Responsiveness Scale ratings) could not be adequately addressed due to the small sample size and limited power.

Clinical Implications and Future Directions

The findings of the present thesis suggest that children with NF1 will require screening, prevention and intervention measures for difficulties in the two broad domains of social competence and perceiving, attending to and interpreting social information, especially faces. These findings highlight important tasks for future research – in particular, clinical trials addressing the efficacy of social intervention programs in children with NF1.

In relation to their social competence problems, the present findings would support the inclusion of the Social Competence with Peers Questionnaire (Spence, 1995) or other appropriate social screening measures into standardised neuropsychological assessment batteries for children with NF1. Multimodal social interventions targeted at forming and maintaining friendships, which could be delivered at the individual or group level, would also be indicated. In particular, the present findings suggest that interventions with a focus on social motivation and the management of anxiety surrounding social interactions would be of benefit.

In relation to general face processing impairments, the present findings of this thesis would indicate that a measure of face perception such as the Facial Recognition Test (Benton, Sivan, Hamsher, Varney, & Spreen, 1994) should also be incorporated into neuropsychological testing batteries for children (and adults) with NF1. At the intervention level, children (and adults) with NF1 are likely to require explicit instruction and practice aimed at teaching them how to attend to and interpret information from faces (e.g. emotional expressions) in their environment. Programs designed to teach these skills in children with autism – for example, FaceSay (Hopkins et al., 2011) – should be clinically trialled to determine their effectiveness for this population. Indeed, more general social interventions

designed for children with ASD would also represent a logical starting point for researchers aiming to select and/or adapt programs to trial in children with NF1. Researchers and clinicians would need to consider the clinical, neuropsychological and social heterogeneity in this population in selecting children who would be most likely to benefit from particular social interventions. Specific assessment of ASD and social anxiety disorder symptomatology as well as face perception abilities would be necessary pre-screening measures to provide more targeted intervention.

Other directions for future research have been highlighted extensively throughout Papers 1, 2 and 3. In particular, studies exploring relationships between social competence and parent- and self-perceptions of quality of life in children with NF1 would be an important continuation of the present thesis to determine whether social competence problems are associated with actual distress in this population. Peer perceptions of factors contributing to social competence problems in children with NF1 would also be important to assist in designing interventions with functional implications in addressing these factors. It would also be important to investigate whether children with NF1 displayed reduced attention to faces under other experimental conditions – for example, when viewing dynamic face stimuli or when given an explicit social-cognitive task to complete with concurrent scan path recording. Such studies would provide useful information regarding social information processing in those with NF1 in more naturalistic ("real world") settings. Furthermore, studies combining scan path recording and functional neuroimaging methods would undoubtedly be of benefit to explore the neurobiology underlying social information processing problems in children with NF1. Finally, it would also be interesting to investigate social functioning and attention to faces in the adult NF1 population.

Concluding Remarks

In summary, the key findings of this thesis were that: 1) children with NF1 displayed social competence problems, even in the absence of comorbid psychopathology; 2) children with NF1 and high levels of ASD symptomatology were at particular risk of social competence problems; 3) socially anxious or avoidant behaviour in NF1 was significantly associated with social competence problems; 4) children with NF1 displayed poor recognition of negative emotional expressions, particularly fear; 5) children with NF1 had difficulty perceiving and discriminating between faces at the basic visuoperceptual level; and 6) children with NF1 spent less time attending to faces, both when presented in isolation and in the context of a social scene. These findings strongly suggested a need to incorporate screening, prevention and intervention for social dysfunction into the general clinical management of children with NF1, with a particular emphasis on attending to and interpreting information from faces. The current thesis extended the existing literature on social functioning in NF1 and also contributed some novel findings regarding specific social information processing deficits in this population.

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