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Neuropsychiatric differences among adolescents with early and late onset conduct, and externalizing and internalizing disorders presenting to a specialist service.

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STATEMENT OF AUTHENTICATION

This thesis is submitted to the University of Sydney in fulfillment of the requirement is for the Degree of Master of Philosophy

The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.

Signature:……………………………………… Date:…26 June 2014…………………

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Abstract

Objective: The conventional view of mental disorders in childhood as discrete and distinct, categorical conditions has been challenged by evidence that suggests many disorders are often comorbid and exist on a continuum. The two papers presented in this thesis investigate whether some disorders in childhood are distinctive in their aetiology and development. This line of enquiry is then extended to broader domains of child and adolescent mental disorders. The first paper focuses on psychiatric illness, neuropsychological and psychosocial dysfunction within the domain of externalizing disorders, examining differences between early and late onset conduct disordered (CD) youth. The second paper examines differences in neuropsychological and psychosocial function between the domains of externalizing and internalizing youth.

Method: Paper one compares the psychiatric, neuropsychological and psychosocial function of forty-three subjects (34 males, 9 females, mean age = 15.31, age range 12-21), with either childhood-onset (n = 23), or adolescent-onset (n = 20) CD. Paper two examines neuropsychological and psychosocial function across the two domains of externalizing and internalizing disorders. One-hundred and forty-eight subjects (81 males, 67 females, mean age = 14.5, age range 12-16) diagnosed with either an externalizing disorder (n=32), internalizing disorder (n=80) or comorbid externalizing/internalizing disorder (n=36) were compared on a range of neuropsychological and psychosocial measures. Participants were compared with normative scores from control samples in each study.

Results: The first study shows differences between childhood-onset and adolescent onset CD youth for verbal learning and memory function, psychosis, childhood maltreatment and violent behaviour with childhood onset youth performing worse on these measures. Both childhood and adolescent onset CD youth were impaired in executive function. The second study found significant differences between the externalizing disordered youth and both the

internalizing and comorbid youth on executive function, with the externalizing youth exhibiting severe impairment in this area or cognitive function. However, when the three groups were corrected for gender, there were no significant differences on executive function, with the group mean for externalizing disorders remaining in the severely impaired range.

Conclusion: Childhood onset CD is associated with more severe cognitive impairment, more psychiatric symptoms and childhood adversity than adolescent-onset youth. They were also more likely to commit serious, violent offences. When CD youth were included in a larger externalizing sample and compared with internalizing and comorbid youth, distinctiveness between the domains remained for some cognitive functions, specifically executive function, but only when females were included. These results emphasize the importance of aetiology and developmental pathways in understanding childhood mental disorders. The findings highlight a need for further research exploring dimensions within each of the domains of externalizing and internalizing, as well as gender differences in childhood developmental disorders.

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INTRODUCTION

Research into childhood psychopathology has generally focused on two broad-band categories, termed "Internalizing" and Externalizing" as a way of identifying childhood behaviour problems [73]. Externalizing disorders are typified by substance use disorders, delinquency and anti-social disorders [76] and include oppositional defiant disorder (ODD); conduct disorders (CD, and attention deficit hyperactivity disorder (ADHD). Within the externalizing domain, high rates of neuropsychiatric disorders have been reported in juvenile populations and are thought to play a role in the development and maintenance of violence and aggression in delinquent samples [77], [1-8], [13], [78]. Heterogeneity within the externalizing population has tended to obscure developmental processes and pathways of psychopathology. Relationships between risk factors and the development of neuropsychiatric disorders alongside antisocial behaviour have limited investigations. One approach in reducing the heterogeneity of this population has been to make distinctions between problems beginning in childhood versus those beginning in adolescence [7], [78], [80]. Age of onset is considered to be associated with different aetiologies with childhood-onset delinquent youth more vulnerable to risk factors across multiple domains; such as neuropsychological dysfunction [32] - [33] mental health problems, poor parenting [34], substance use disorders [11], learning difficulties and poor school attendance [35], head injuries [36], [32] - [33] and childhood maltreatment and trauma [37] - [38]. Conversely, associating with delinquent peers has been thought to predict delinquency commencing in adolescence [39].

Studies have investigated differences within this developmental typology through both pathways and cross-sectional analysis. However few longitudinal studies exist that follow the course of psychopathology and its relationship with antisocial behaviour from

adolescent into adulthood. The bulk of research supports the hypothesis that these different aetiologies, also predict different outcomes [7], [40]. However, recent studies have queried Moffit's dual taxonomy with similar neurophysiological profiles found in both childhood and adolescent onset CD. Fairchild et al. [28] found impairments in emotional processing and fear conditioning in both CD subgroups, and Roisman, et al. [30] found social disadvantage from infancy for children who showed antisocial behaviour primarily in adolescence, challenging assumption that adolescent-onset CD is normative. Fairchild and colleagues [29] argue that differences between the two subtypes of antisocial behaviour might be quantitative rather than qualitative

Problems with heterogeneity continue to exist in the literature, even after correcting for age of onset of antisocial behaviours. This is due mostly to high rates of comorbidity within this population, for example, rates of co-occurrence between CD and ADHD range up to 90% [81] - [83]. Additionally, many studies have focused on incarcerated 'delinquent' youth within singular domains of function. Few studies have examined young people with a diagnosis of conduct disorder, which requires meeting a more stringent criterion. Issues relate to "lumping together young people who are temporarily experimenting with mild delinquent acts with young people whose antisocial behaviours are more serious, persistent or physically aggressive" [31, p. 136] in delinquent samples potentially weakening differential effects.

The first study presented in this thesis investigates function across a number of domains: psychiatric, neuropsychological and psychosocial, in community-based, conduct-disordered youth. It will test the validity of Moffitt's (1996) model by examining variability in neuropsychiatric function, violent behaviour and social disadvantage between the two CD

subtypes. It hypothesizes that the childhood-onset CD youth will have more severe psychiatric symptoms, neuropsychological deficits, including verbal and executive deficits in particular, higher frequency of childhood adversity and more serious violent behaviour than adolescent-onset CD peers.

The second study takes a broader perspective of childhood behavioural problems by examining neuropsychological and psychosocial function between the externalizing and internalizing domains. There is evidence of high comorbidity between and within the domains. Rates of comorbidity between disorders within the externalizing domain range from 29% to 71% [84]. This has also been demonstrated through epidemiological studies [22], [85]-[89]. Similarly, substantial overlap exists between the internalizing disorders, which comprise mood and anxiety problems [90]. Co-occurrence between the externalizing and internalizing domains has been highlighted in a number of studies although the strength of associations has differed [14] - [17]. Some investigators argue that variability in association strength may relate to differences between clinically referred adolescents and adolescents from the general population, as clinical samples are more likely to have multiple disorders [91].

Overall, findings suggest that there may be common factors that predispose individuals to externalizing and internalizing disorders. Neuropsychological studies have found evidence for frontal lobe and executive dysfunction in childhood and adolescent ADHD [92] - [98]. Executive function deficits have been linked with antisocial behaviour [99] - [105]. Earlier delinquent studies [6] identified deficits in three areas: executive function, language abilities and cerebral dominance. However many of these studies did not assess cognitive functions simultaneously.   Later studies using a broad range of

neuropsychological measures found impairments in memory, even after excluding executive function [106].

Neuropsychological findings for internalizers have been less consistent with some investigations identifying higher verbal and full scale IQs when compared with externalizers [107] and reduced functioning in attention, concentration, working memory in both verbal and visual tasks, and processing speed in depression. However, cognitive function returns to premorbid levels after an episode of depression resolves [108]. In overanxious and obsessive compulsive disordered (OCD) adolescents, deficits have been found in executive function, visual memory, attention and processing speed [109] - [110]. Less is known about the neuropsychological profiles of young people with a comorbid externalizing/internalizing disorder.

The objective of this analysis was to understand whether fundamental differences in neuropsychological function exist for young people with externalizing problems when compared to young people with internalizing problems. Most of the research in this area has examined symptom progression and developmental pathways [17], [111]. The literature has also been less clear about neuropsychological function in the internalizing disorders as neurocognitive deficits may be transient and episodic. Few studies have focused on neuropsychological function underlying the two domains. By assessing clinical symptoms alongside neuropsychological function in cross-sectional analysis, important insights may be gained into brain-behaviour relationships. The objective of this analysis was to determine whether externalizing disordered youth would have higher rates of neuropsychological deficits, including verbal and executive deficits, than internalizing youth and whether there are high rates of comorbidity between the externalizing and internalizing domains.

This thesis aims to incorporate findings from both studies into a coherent understanding of neuropsychiatric disorders in adolescence, challenging the categorical nature of current diagnostic methodologies. By examining neuropsychiatric differences between the externalizing and internalizing domains and then taking a more detailed investigation into the externalizing subgroup of conduct disorder, the notion of dimensionality of disorders will be explored to determine whether a dose-response type relationship exists between deficits and disorder.

CHAPTER 1

Childhood- versus Adolescent-Onset Antisocial Youth with Conduct Disorder: Psychiatric Illness, Neuropsychological and Psychosocial Function

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Abstract

Objective: The present study investigates whether youths with childhood-onset antisocial behavior have higher rates of psychiatric illness, neuropsychological and psychosocial dysfunction than do youths who engage in antisocial behavior for the first time in adolescence. Prior studies have generally focused on single domains of function in heterogeneous samples. The present study also examined the extent to which adolescent-onset antisocial behaviour can be considered normative, an assumption of Moffitt's dual taxonomy model.

Method: Forty-three subjects (34 males, 9 females, mean age = 15.31, age range 12–21) with a diagnosis of conduct disorder (CD) were recruited through Headspace Services and the Juvenile Justice Community Centre. We compared childhood-onset antisocial youths (n = 23) with adolescent-onset antisocial youths (n = 20) with a conduct disorder, across a battery of psychiatric, neuropsychological and psychosocial measures. Neuropsychological function of both groups was also compared with normative scores from control samples.

Results: The childhood-onset group displayed deficits in verbal learning and memory, higher rates of psychosis, childhood maltreatment and more serious violent behavior. Both groups had impaired executive function.

Conclusions: Childhood-onset CD displayed greater cognitive impairment and more psychiatric symptoms and committed more serious violent offences. The finding of severe executive impairment in both childhood- and adolescent-onset groupings challenges the assumption that adolescent-onset antisocial behavior is a normative process.

Key words: delinquency, violence, antisocial behavior, conduct disorder, neuropsychiatry

INTRODUCTION

Findings in the youth offender literature indicate that psychiatric symptoms, neuropsychological deficits and psychosocial factors play a role in the aetiology and maintenance of violence and aggression [1]–[5] (see [6]–[7] for reviews). However, the extant literature is characterized by a variety of limitations [8] including a focus on adult incarcerated populations, defining age of onset by first criminal charge (rather than initial behavioral difficulties), disorder heterogeneity and a focus on discrete and singular domains of function (rather than a profile of deficits). Here we examine differences between adolescents with either childhood- or adolescent-onset conduct disorder across a battery of psychiatric, neuropsychological and psychosocial measures.

The Prevalence of Mental Illness in Violent Offenders

Mental health problems are over-represented amongst incarcerated adults and youths in several countries, with rates higher than in the general community [9]–[13]. High rates of psychiatric comorbidity have been reported in child and adolescent community samples [14]–[17], and the prevalence of risk factors such as substance use [18]–[21] and a history of violence [22], [23] are also high.

Neuropsychological Deficits in Delinquent Youth

Areas of cognitive function most frequently identified as showing deficits in delinquent youth include IQ, verbal learning and memory and the executive functions [7], among subjects with CD [24], [8], adolescent girls [25], [26] and those with comorbid bipolar disorder [27]. However, few studies have addressed problems associated with heterogeneity. Childhood- and adolescent-onset CD is often combined into a single group,

and other disorders such ADHD may influence findings, factors taken into consideration in the present study.

Developmental Pathways in CD and Associated Psychopathology.

There is a need to focus on different developmental pathways of psychopathology and how they relate to criminal and violent behaviour. Different aetiologies or developmental trajectories can lead to be similar outcomes in adulthood. Mentally ill offenders are a heterogeneous group, with varying relationships between risk factors as well as the development of both the primary disorder and the antisocial behaviour. In order to study the aetiology of criminal and violent behaviour of persons with developing mental health disorders, it is necessary to adopt a developmental perspective which examines the continual interaction of biological, psychological and social factors over the course of an individual's life.

Raine and colleagues [112] proposed four models to explain interaction between biological and social factors. They suggest that biological and social risk factors may come together in a correlated, additive, sequential or multiplicative way. Other developmental perspectives include; Hofstra et al [113] model with a focus on the duration of maladapted functioning, and Arseneault, et al [114], Hodgins et al [115] and Rutter et al [116] models of trajectories of antisocial behaviour and mental illness, describing distinct patterns of criminality and violence among persons with schizophrenia. These developmental models, consider childhood deviant behaviour as a prodrome to schizophrenia rather than the development of conduct problems and schizophrenia as two distinct diagnostic entities [117].

Life-Course Persistent Offenders versus Adolescent-Onset Offenders

Moffit's dual taxonomy model [7] proposes that different aetiologies and developmental courses define the onset of offending. According to this model, life-course persistent antisocial behavior begins in early childhood and continues throughout adulthood, while offenders with adolescent-onset antisocial behavior desist in young adulthood. However, recent studies [28]–[30] have questioned this theory by showing similar neurophysiological profiles in both childhood- and adolescent-onset CD. For instance, Fairchild et al. [28] found impairments in emotional processing and fear conditioning in both CD subgroups, and Roisman et al. [30] found social disadvantage from infancy for children who showed antisocial behavior primarily in adolescence, challenging the assumption that adolescent-onset CD may be normative. These authors suggest that revision of the model of the development of antisocial behavior may be necessary. The current study, therefore, sought to test the validity of Moffitt's [31] model by examining variability in violent behavior and neuropsychiatric function.

Risk Factors for Antisocial Youth

According to Moffit's taxonomical model, childhood-onset antisocial youth will be more vulnerable to risk factors across multiple domains including neuropsychological dysfunction [32], [33], mental-health problems, poor parenting [34], substance use disorders [11], learning difficulties and poor school attendance [35], head injuries [36], [32], [33] and childhood maltreatment and trauma [37], [38]. Moffit's review [6] across 47 studies, found that antisocial youth, in general, were impaired in two specific cognitive domains: language-based verbal skills and "executive" self-control functions. These studies found strong effect sizes even when "young people who are temporarily experimenting with mild delinquent

acts are lumped together with young people whose antisocial behaviors are more serious, persistent or physically aggressive" [7 p. 136]. However, these two groups could be further conceptualized as youth with varying risk. The greater the number of risk domains, the higher the risk of violence, as violence is the "end product of a chain of events over the course of a child's development, where risks accumulate and reinforce each other" [40, p. 181].

More recently, Fairchild et al. [41] reviewed the developmental taxonomic theory of antisocial behavior, reporting that both CD subtypes display emotion-processing deficits, changes in brain structure and function, as well as alteration in cortisol secretion.

Research in this field clearly indicates that neuropsychiatric and developmental risk factors are integral to the aetiology of aggression and violence. However, many investigations into antisocial youth have struggled with disorder heterogeneity. Delinquency research has not always accounted for comorbidity, with dual diagnoses of conduct disorder and ADHD resulting in the poorest outcomes and strongest predictors of adult crime [7].

The current study examines psychiatric, neuropsychological and psychosocial risk factors in non-institutionalized samples. It was hypothesized that childhood-onset CD youth would display more severe psychiatric symptoms, neuropsychological deficits, including verbal and executive deficits in particular, and higher frequency of family dysfunction and child maltreatment than their adolescent-onset peers. Furthermore we expected that the early-onset group would be characterized by more violent behavior than the adolescent-onset group.

METHOD

Participants

Forty-three young people (age range: 12–21 years, M: 15.31, SD: 2.3; gender: M: 34, F: 9) who had engaged in violent and antisocial behavior were recruited for this study through Headspace Services (n=28) – a group specializing in the assessment and early intervention in mental health problems in young people [42], [43] – and a Juvenile Justice Community Centre (n=15). Sampling from two relevant service providers allowed a sufficient sample to be recruited, and provided a broader spectrum of people with actual offending and mental-health problems. Inclusion criteria included persons aged between 12 and 21 years and DSM-IV-TR criteria for a diagnosis of conduct disorder (CD). All young people included in the study were living in the community, either within their family homes or in non-government run group homes for young people.

Ethics Statement

This study protocol was approved by the Human Research Ethics Committee at the University of Sydney (Ref No. 02-2009/11107). Participants were informed that participation was entirely voluntary, and if they agreed to participate, that they were able to withdraw consent at any phase of the study without prejudice. Participants 18 years and older were required to sign a "Participant Consent Form", while parents or guardians of participants under 18 years of age were required to give written consent via the "Parental (or Guardian) Consent Form" alongside consent of the child. Participants and their legal guardians were informed of the limits of confidentiality regarding offending behavior, via the information sheet provided, as well as a script read aloud to participants prior to the commencement of the clinical interview. All participants under the Juvenile Justice System

were accompanied by a caseworker, who provided additional information regarding a participant's capacity to consent. If mental-health problems were identified during the assessment process for a participant, they were offered information regarding treatment or referred to a mental-health clinician at Headspace Services, Camperdown.

Procedure

Psychiatric symptoms, neuropsychological deficits and psychosocial risk factors were determined using a variety of measures, which are described below. A psychiatrist or clinical psychologist conducted clinical interviews for all potential participants, and a diagnosis of CD was given if DSM-IV-TR criteria for the disorder were met. Age of onset was defined using the DSM-IV-TR [44] criteria based on the presence of three of 15 behavioral criteria, with the presence of one characteristic behavior prior to age 10 differentiating childhood-onset from the adolescent-onset subtype. An absence of any criteria characteristic of conduct disorder prior to the age of 10 years was required to meet the criteria for adolescent-onset subtype. Identification of the childhood-onset group was determined through a series of questions asked during the clinical interview. They were: "When did you first start to get into trouble with police?" "When were you first arrested by the police?" date of first (if any) court appearance; "When did you first start breaking into places; stealing other people's possessions, including breaking into cars?"

Initial attempts were made to collect parent reports on symptom onset, however many young people reported fractured family backgrounds suggesting that parent reports may be unreliable. Other difficulties encountered in collecting parent reports were the non-compliance of the parent or primary carer to complete forms. A number of young people had

Juvenile Justice caseworkers who provided useful information regarding a young person's level of overall functioning.

Young people determined to be child-onset versus adolescent-onset were separated into the two groups with the former group containing 23 subjects, and the latter containing 20 subjects. Demographic information regarding a participant's childhood experience of maltreatment, head injury, family dysfunction and severity of violent behavior was obtained through clinical interview. Evidence for a comorbid diagnosis of ADHD was determined through clinical interview.

Psychiatric Measures

Kessler Psychological Distress Scale-10

The Kessler psychological distress scale (*K-10)* [45] is a widely used, simple self-report measure of psychological distress consisting of 10 items and scored using a five-level response scale based on the frequency of symptoms reported for each question. It is useful in the identification of individuals who need further assessment for anxiety and depression. Scores under 20 are likely to be well. Scores between 25 to 29 are likely to have moderate mental disorder and scores 30 and over are likely to have a severe mental disorder [75]. *Reliability and Validity:* The scale has good construct and criterion validity [118], showing strong association with mental health symptom measures as well as frequency of consultations for mental health problems in a 12-month period [119]. Kessler et al [118] found high levels of sensitivity and specificity with high Cronbach's alpha (.93).   The K-10 was hand scored by research psychologists.

Depression Anxiety Stress Scale 21

The Depression Anxiety Stress Scale 21 (DASS) [46] is a valid and reliable measure of depression, anxiety and stress separately [47]. Each of the three DASS-21 scales contains seven items, divided into subscales with similar content. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale is sensitive to levels of chronic non-specific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. Scores for depression, anxiety and stress are calculated by summing the scores for the relevant items. The DASS-21 was administered to determine mild = 0-4/moderate = 5-9/severe =6 - 10/extremely severe scores = 11+ for each DASS scale. *Reliabilty and Validity:* The DASS-42 has excellent internal consistency and test-retest reliability and can distinguish between features of depression, physical arousal and psychological tension and agitation better than other existing measures [120], [119], [46]. This was confirmed in later studies and extended to apply to the DASS-21 [121], [119]. Cronbach's alphas for the DASS-21 subscales were 94 for Depression, .87 for Anxiety and .91 for Stress.

Hamilton Depression Rating Scale

Hamilton Depression Rating Scale (HAM-D) is a clinician-administered rating scale to assess symptom severity in depressive disorders. Symptoms are rated on a severity scale in individuals otherwise diagnosed with depression. It is a questionnaire used to provide an indication of depression and as a guide to evaluate recovery. Although the HAM-D form lists 21 items, the scoring is based on the first 17 items. Eight items are scored on a 5-point scale, ranging from 0 = not present to 4 = severe. Nine are scored from 0–2. A score of 0–7

is considered to be normal. Scores of 16 or higher indicate full symptomatic status [41].

Reliability and Validity: Trajkovic [122] found a pooled mean for alpha coefficients in random effects model was 0.789 (95%CI 0.766-0.810) suggestive of good levels of internal consistency. Inter-rater reliability, pooled means in random effects model were 0.937 (95%CI 0.914-0.954) for the intraclass correlation coefficient, 0.81 (95%CI 0.72-0.88) for the kappa coefficient, 0.94 (95% CI 0.90-0.97) for the Pearson correlation coefficient, and 0.91 (95%CI 0.78-0.96) for the Spearman rank correlation coefficient. Test-retest reliability ranged between 0.65 and 0.98 and generally decreased with extending the interval between two measurements. These results suggest that the HAM-D provides a reliable assessment of depression. The HAM-D showed adequate convergent validity in correlations with all but two scales, including the major depression section of the Structured Clinical Interview for DSM-IV [123]. Discriminant validity: Zheng et al [123] reported that the HAM-D was able to discriminate psychiatric patients classified as mildly, moderately and severely dysfunctional.

Brief Psychiatric Rating Scale

The Brief Psychiatric Rating Scale (BPRS) [48] is a 24-item scale for the identification and quantification of psychiatric symptoms. The instrument contains 24 ordered category-rating scales to assess positive and negative symptomatology in discrete symptom areas. The BPRS is a sensitive and effective measure both of psychopathology and of treatment-related symptom changes [76].. Suggested cut-off scores for the BPRS have usually related to the total score rather than sub-scales. A range of 31 to 40 relates to a "minimally ill" level of psychological distress; 41 to 53 relates to "moderately ill"; and above 53 is considered "markedly ill" level of psychological distress [49]. The BPRS Total score will therefore be used to determine cut-offs for the two groups. A review of published

studies of the BPRS reported interrater reliability for the total pathology score at 0.80 or greater for 10 out of 13 studies. The median reported Pearson correlation for individual items ranged from 0.63 to 0.83 in 5 studies [216]. The reported validity of the BPRS is generally high when compared with other measures of general psychopathology [217].

Neuropsychological Measures

Trained research psychologists administered a battery of neuropsychological tests covering a number of cognitive domains including Intellectual Ability, General Knowledge, Processing Speed, Simple Attention, Sustained Attention, Working Memory, Learning & Memory − Verbal, Learning & Memory − Visual, Visual Spatial, Executive Functioning, Cognitive Flexibility, Executive Functioning − Verbal Fluency. Measures were combined into composites if they measured similar areas of cognitive functioning. Test scores were converted to z-scores to ensure common means and standard deviations and then summed and averaged. All the tests had recent norms that are representative of the age and educational status for the population under investigation. All the instruments were well standardized, reliable and validated in prior studies. The test battery was designed to assess: intellectual ability, speed of information processing, working memory, executive function, planning and organization, simple and sustained attention, visual spatial skills, visual and verbal learning and memory and processing speed.

Wechsler Test of Adult Reading

The Wechsler Test of Adult Reading *(WTAR)* [52] consists of a word reading list and estimates IQ. It has been co-normed with the third editions of the Wechsler Adult Intelligence and Memory Scales. The WTAR also has the advantage of offering three methods by which to estimate IQ, based on reading performance, demographic information

or a combination of the two.   In the design of the WTAR, the demographic prediction tables were co-normed with the widely used Wechsler Adult Intelligence Scale (WAIS) and Wechsler Memory Scale (WMS). The *Wider Range Achievement Test R (WRAT-R)* [53] is the child version of academic achievement, administered to participants 16 years and younger. *Validity and Reliability:* The WTAR shows excellent internal consistency for the various age groups, with coefficients ranging from .90 to .97 for the U.S. standardization sample and from .87 to .95 for the U.K. sample [124]. Test-retest reliability is fairly stable over time. Test-retest correlations were very good (>.90) and practice effects were minimal in a sample of 319 participants over a 12-week period (Strauss, et al., 2006). The WTAR shows high correlations with other measures of reading (e.g. American National Adult Reading Test (AMNART) [125], r = .90; WRAT-R, r = .73; WTAR, 2001).

The *Wider Range Achievement Test R (WRAT-R)* (Jastak & Wilkinson, 1984) is the child version of academic achievement, administered to participants 16 years and younger. The word pronunciation format of the test is identical that of the National Adult Reading Test-Revised (NART-R) [126]. Use of the WRAT-R Reading for premorbid prediction compares favorably to regression-based procedures [126].

Wechsler Adult Intelligence Scale-III

The Wechsler Adult Intelligence Scale-III (WAIS-III) *Information i*s a subscale of the verbal IQ score and is a measure of general knowledge. The *Wechsler Intelligence Scale for Children-III (WISC-III) Information* was administered to participants 16 years and younger. *Validity and Reliability:* Average reliability coefficients for the WAIS-III are high for most of the individual subtests and range from .93 to .70. Internal consistency figures for Information range from .89 to .93 across age groups. Average stability coefficients for

Information are excellent [126]. Inter-rater reliability is reported to be high (>.90) [126].

There is substantial correlation (.80 and above) between the WAIS-III and its predecessors.

Trail-Making Test

The Trail-Making Test (TMT) is a measure of attention, speed and mental flexibility. It consists of parts A and B. Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1–25, and the patient is required to draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A–L); as in Part A, the participant draws lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1–A–2–B–3–C, etc.). The participant should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Part B of the TMT has been found to be the most sensitive to frontal damage and involves the ability to alternate between, and maintain, two sets of stimuli [54]. *Reliability and Validity:* Dikemen [127] found coefficients were adequate for Part A (.79) and high for Part B (.89). Levine et al [128] also found adequate coefficients (.70 for A and B). Inter-rater reliability has been reported as .94 for Part A and .90 for Part B. Good validity had been reported in terms of the TMT's sensitivity to neurocognitive deficits and localized brain dysfunction, particularly frontal lobe abnormalities [129]-[130]

Controlled Oral Word Association Test

Controlled Oral Word Association Test, abbreviated COWA or COWAT, is a verbal fluency test that measures spontaneous production of words belonging to the same category or beginning with some designated letter. The participant is asked to name words beginning

with a letter, excluding proper nouns, for one minute and this procedure is repeated three times. The most common letters used are F, A, and S because of their frequency in the English language. The examiner must quickly write down the words provided by the participant on a piece of paper. Word generation has been found to be a reliable test of left frontal and executive functions [55]. The Controlled Oral Word Association Test [56] evaluates the spontaneous production of words under restricted conditions. *Reliability and Validity:* Tombaugh et al [131] found internal consistency to be high (.83). In healthy adults, test-retest correlations tend to be high, above .70, for short (one week) as well as long (five years) intervals [127]-[128]. Inter-rater reliability is high (.99) [139] and (.98) [139]. The instrument reports good validity [139].

Cambridge Neuropsychological Test Automated Battery

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computer-administered, nonverbal (visually presented) set of tasks developed to examine specific components of cognition. The software comprises one screening test and 12 principal tests from the CANTAB system [57]–[59]. The CANTAB is designed to test different aspects of mental functioning so that a profile of performance can be constructed, including independence of executive measures and memory factors [60]. The CANTAB subtests consist of: spatial span, choice reaction time, rapid visual processing, intra/extra-dimensional shift and paired associated learning. The test scores are computer generated and give a rating from impaired to high average for: simple and sustained attention, visual and verbal learning and memory, working memory, speed of information processing, visual spatial skills and executive function. *Reliability and Validity:* Internal consistency was reported to be adequate to high, ranging from .73 to .95 in a sample of 4- to 12- year old children [134]. Many of the CANTAB measures were found to have poor test re-test

reliability [135]. Lowe et al [135] stressed that the tasks may not be poorly defined or ill chosen but rather, excellent tests of executive ability may depend for their sensitivity on their novelty, restricting their use to a single occasion. Robbins [136] examined the factor structure of some of the CANTAB subtests (Paired Associate Learning, Delayed Matching to Sample, Pattern Recognition, Matching to Sample, Spatial Working memory, Stockings of Cambridge (Tower of London), Spatial Span, Spatial Recognition, Intra/Extradimensional Shift) and found evidence for a six-factor model and found considerable independence among the different executive measures and separation of executive and memory factors.

Verbal memory

Immediate and delayed verbal memory was measured using the Logical Memory subscale of the Wechsler Memory Scale (WMS-III) [61].]. Participants were required to recall stories A and B after a 30-minute delay. The examiner records the number of free recall and thematic units. *Validity and Reliability:* Validity studies are strongly positive [137]. However available data provide no statistical support for separate immediate and delayed indices in either normal or clinical samples. The reliability of WMS-III subtests and indices tends to be adequate to high. The median reliability of subtests is .81 and .87 for Indices. Supplemental subtest scores are lower at .77, but still adequate [138]. The majority of the indexes have stability coefficients in the .80s. Logical memory I and II range from .71 to .91 across age groups [139].

Rey Auditory Verbal Learning Test

The Rey Auditory Verbal Learning Test (RAVLT) is a test of memory where the examiner reads a list of 15 concrete nouns. The examinee recalls as many as possible in any

order through five administrations and a recognition trial. It allows for the identification of

memory impairment and is a measure of verbal memory. *Validity and Reliability:* Vakil &

Blachstein [126] identified two basic factors that they interpreted as reflecting acquisition

and retention. Mueller et al. [126] distinguished between short-term memory and long-term

latent memory in two heterogeneous clinical samples. Rosenberg et al [141] found the

RAVLT performs well in the identification of patients known to be memory impaired by

other criteria. The RAVLT correlates moderately with other measures of learning and

memory such as the WMS-R Logical Memory and Visual Reproduction subtests [126] and

the CVLT [126]. The RAVLT is sensitive to neurological impairment [126], laterality of

brain damage [126] and memory deficits in a variety of patient groups [126]. Internal

reliability is high, with (coefficient alpha) of the total score at .90 [126]. The test-retest

reliability is marginal /adequate over a 1 year period [126]. Practice effects reduce with

different RAVLT versions [126].

Psychosocial Measures

Social and Occupational Functioning Assessment Scale

Psychosocial factors were measured on the Social and Occupational Functioning

Assessment Scale (SOFAS) and various items on the semi-structured interview. The *SOFAS*

is a clinician-administered measure of problems in social, occupational and interpersonal

functioning. It measures the frequency of social activities across seven subscales:

withdrawal/social engagement, interpersonal communication, independence-performance,

independence-competence, recreation, prosocial and employment/occupation. It focuses

exclusively on the individual's level of social and occupational functioning and is not

directly influenced by the overall severity of the individual's psychological symptoms [44].

Reliability and Validity: Strong support has been found for the reliability and validity of the

SOFAS [142]-[144].   Birchwood et al [142] found high internal reliabilities (coefficient alpha) and strongly differentiated criterion groups with SOFAS scores correlated with the presence of both negative (r = -0.44) and positive (r = -0.46) symptoms based on assumptions that negative symptoms contribute to deficits in social functioning. Hilsenroth [145] found the SOFAS exhibited very high levels of inter-rater reliability and factor analysis revealed the SOFAS is a good measure of problems in social, occupational and interpersonal functioning.

Severity of Dependence Scale

Participants were also administered the Severity of Dependence Scale (SDS) [62], which is a short, clinician-administered rating scale used to measure the degree of dependence experienced by users of different types of drugs. The SDS contains five items, all of which are explicitly concerned with psychological components of dependence. These items are specifically concerned with impaired control over drug taking and with preoccupation and anxieties about drug use. Higher scores indicate higher levels of dependence. It is primarily a measure of compulsive use, which is a central component of dependence. *Reliability and Validity:* Good internal consistency (ranging from .8 to .9) has been reported across five samples and good test-retest reliability (.89) over a one-day interval in a sample of heroin users [146], [147].   Construct validity is supported by significant correlations with behavioural indices of dependence including dose, frequency and duration of use [147]. One study found only a moderate level of internal consistency for cannabis dependance (alpha = .72) [147].   Item correlations were statistically significant from .45 to .69 (p<.01)

Family Dysfunction Measures

Three household dysfunction variables were used in the study: Household mental illness, Household substance use disorders and Household learning disability, all binary, self-report measures. Each variable is comprised of information taken from the subject's family history. Many participants tended to be poor historians, therefore it was difficult to quantify the number of family members affected and the severity of the disorder for each family member on each variable.

Household mental illness refers to the degree of mental-health problems in the young person's immediate family. Mental-health problems include mood and psychotic disorders.

Household SUDS refers to the incidence of drug and alcohol use in the young person's immediate family.

Household learning disability refers to the incidence of learning disabilities, including autism spectrum disorders and Asperger's disorder in the young person's immediate family. There were a number of self-report measures taken during the clinical interview that were included in the analysis as binary social/environmental variables. These include: *Childhood physical abuse, Incidence of head injury, Substance use and School attendance.*

Severity of conduct disorder

A binary variable measuring the degree of aggression and violence the young person has engaged in. This measure relates to the "Severity Specifiers" for conduct disorder categorization in the DSMIV-TR.

Level 1 is a mild to moderate level of violence and antisocial behavior and includes damage to property, initiating physical fights either in the home and school, bullying and threatening behavior; truanting from school, school suspensions and expulsions, aggression toward others.

Level 2 is a more severe level of violence and antisocial behavior and includes serious assaults leading to charges and convictions. Offences include break and enter, use of a weapon, armed robbery and attempted murder.

Data and Statistical Analysis

All statistical analyses were performed using SPSS, version 20 (SPSS Inc., Chicago, Illinois, USA). The various psychiatric, neuropsychological and psychosocial variables were subjected to independent t-test (continuous variables) and chi square (for categorical variables) analyses to determine whether early- and late-onset antisocial youth could be distinguished on specific risk factors identified in the literature. Significant effects were set at $p < .005$ for *t* tests and chi-square after applying a Bonferroni correction for repeated tests and small cell sizes. Participants were excluded from the study at the point of statistical analysis if they were identified as an outlier deemed to be 1.5 times the interquartile range on all neuropsychological measures. All language-based neuropsychological tests were corrected for years of education within standardized scoring calculations and were appropriately normed. Cohen's d effect size statistics were calculated for each pair-wise comparison. Cohen's guidelines [63], [64] identify 0.2, 0.5, and 0.8 as small, medium, and large effects, respectively. Odds ratios were calculated for chi square statistics indicating the degree of association between binary variables. The statistical threshold of 0.005 (two-tailed) was set for all analyses.

Neuropsychological Composites

Composite measure of executive function: A composite measure of variables was created using the SPSS "compute variable" procedure to measure the construct "executive function" across the delinquency group. Three neuropsychological tests, namely Trail Making Test A and B, Intra/Extra Dimensional shift and COWAT animals and letters were included in the composite as they each measure various aspects of executive function [55]. The Trail Making Test A and B measures visuo-motor tracking, divided attention and cognitive flexibility and is sensitive to frontal lobe lesions [50]. Word fluency and the generation of word lists on the Controlled Oral Word Association Test, F-A-S, is a sensitive indication of brain dysfunction, particularly within the frontal area. People with frontal-lobe lesions have reduced letter and category fluency and therefore deficient retrieval strategies. Intra-extra Dimensional Shift is a test of rule acquisition and reversal. It measures the visual discrimination, attentional set formation maintenance, shifting and flexibility of attention and, therefore, is primarily sensitive to changes in the frontal areas of the brain [65].

In factor analytic studies, Intra-extra Dimensional Shift was found to measure attentional set formation, maintenance and shifting, Trail Making Test-A required mainly visuo-perceptual abilities and Trail Making Test-B primarily reflected working memory and secondarily task-switching ability. The Trail Making Test was found to have construct validity for task switching, working memory, inhibition/interference control and visuomotor abilities [72]. Duff et al. [73) found a strong relationship between executive functioning and memory capacities as measured by the Controlled Oral Word Association Test and Trail Making Test A and B and that they shared more than 50% of variance.

Composite measure of auditory verbal learning and memory (RAVLT): Comprised items on the Rey Auditory Verbal Learning and Memory test: RAVLT sum, A6 and A7 and produced through the SPSS "compute variable" procedure. A6-A7 measures susceptibility to proactive and retroactive interferences and correlates moderately with measures of immediate recall (Sum A1-A5) [73].

Psychiatric Composite

The BPRS Total score was used as a general measure of psychiatric symptoms.

Psychosocial Composite

Composite measure for family dysfunction: Comprised the three Household Dysfunction measures: Household mental illness, Household SUDS and Household learning disability, which were manually collated from the categorical dataset.

RESULTS

Participant Characteristics

Among the 43 young persons assessed (age range: 12–21 years, M: 15.31, SD: 2.3; gender: M: 34, F: 9), no significant differences between age-of-onset groupings were found regarding the subject's age at assessment ($t(41) = -1.02$, p=.31), or for diagnosis of ADHD $\chi2(2, N=43)=4.6$, *p*=.10). Of the 23 early-onset youths, 16 were diagnosed with comorbid ADHD. The late-onset group, comprising 20 participants had 13 individual with comorbid ADHD. It was necessary to control for ADHD as it is a disorder associated with severe impairment in executive function. It is also highly comorbid with CD. If ADHD was not controlled for, it would be difficult to determine whether differences between groups were related to age of onset or presence/absence of ADHD. There were no significant differences

observed between groups for gender, ($\chi2$(1, N=43)=1.8, *p*=.17), with the early-onset group

containing three females versus six females in the late-onset group. Among the youths, those

with early-onset CD had significantly lower levels of education than did the late-onset

youths (t(41)= -2.35, *p*=.02).

Table 1.1. Participant characteristics

	Childhood-onset CD (M ± SD)	Adolescent-onset CD (M ± SD)	Cohen's d
N	23	20	
Gender	M:20 (87%) F:3 (13%)	M:14 (70%) F:6 (30%)	
Age at Assessment	15 ± 2.29	15.75 ± 2.51	.3
Years of Education	8.39 ± 1.67	10 ± 2.75	.71

Subjects Age at assessment Years			Frequency
12	4	1	5
13	2	2	4
14	4	4	8
15	5	5	10
16	2	1	3
17	3	3	6
18	2	1	3
19		1	1
21	1	2	3
Total	23	20	43

Psychiatric data

Groups differed significantly on the BPRS total (t(38)= 2.5, *p*= .01) with the early-onset group exhibiting more psychotic like symptoms, such as hallucinations, delusions, disorientation, mania and negative symptoms. Both groups fell within the "minimally ill" level, however the early-onset group were further along the scale toward the "moderately ill" level. The groups also differed significantly on the YMRS (t(23)= .2.6, p= .001, with both groups falling below the ≤12 cut-off score of threshold symptomatology. No significant differences were observed between the groups on the DASS21, with depression (*t*(36)= .13, *p*= .81, anxiety (*t*(37)= .67, *p*= .83 and stress (*t*(37)= .78. *p*= .76, falling within the moderate to severe range in symptom severity; while both groups fell within the "minimally ill" range on the Kessler-10 (*t*(38)= -.43, *p*= .28, and the HAMD (t(38)= 1.4, *p* = .4.

The groups showed significant differences with regard to "Severity of Conduct Disorder" (χ*2* (1, 43) = 7.3; *p* = .007) and "Contact with Law Enforcement Agencies" (χ*2* (1, *N*=43) = 8.2; *p* = .006) with the early-onset group committing more serious and violent offences [Childhood onset: 14 (77.8%); Adolescent onset: 4 (22.2%)], as well as having more contact with police and the juvenile court system [Childhood onset: 18 (78%)]; Adolescent onset: 8 (40%)]. There were no significant differences for the group regarding "Severity of Dependence-Primary Drug" (χ*2* (3, 43) = 5.0; *p* = .17), and "Head Injury" (χ*2* (3, *N* = 43) = 2.1; *p*= .15),

Neuropsychological data

Groups differed significantly on the RAVLT composite (t(41)= -3.3, *p*= .002) with the early-onset group performing worse on these measures. No significant differences were observed between groups on WTAR/WRAT (t(41)=-2, *p*=.05), WAIS/WISC Information

(t(40)= -1.5, *p*= .15), Choice Reaction Time – simple movement time (t(34)= 1.58, *p*=.12), –

simple reaction time (t(36)= -0.21, *p*=.05), – 5 choice movement (t(36)= -0.21, *p*=.83), – 5

choice reaction (t(36)= -1.24, *p*= .22), Mental Control/Sequences (t(40)= -0.16, *p*=.87),

Rapid Visual Processing A (t(38)= -1.6, *p*=.12), Rapid Visual Processing B (t(35)= -2.0, *p*=

.05), Rapid Visual Processing mean latency (t(36)= -1.7, *p*=.09), Paired Associate Learning-

total errors adjusted (t(39)= -0.94, *p*=.35), Paired Associate Learning-total errors 6 shapes

(t(38)= -0.53, *p*= .59), spatial span length (t(39)= -2.6, *p*=.01), Trail Making Test A (t(39)=

-1.73, *p*=.04 and B (t(41)= -1.5, *p*= .3, Logical Memory 1 (t(17)=-1.2, *p*=.04, 2 (t(17)= -1.9,

p=.04 and Rey Auditory Verbal Learning B1 (t(41)= -1.04, *p*= .4 and Executive Function

composite (t(36)= -1.38, *p*= .17).

Score interpretation for the RAVLT (M = -3.13 and SD = 3.23) for early-onset CD

fell within the Extremely Low (Severely Impaired) range while the late-onset CD fell within

the Average Range score (M = 0.18 and SD = 3.35). Both the early-onset (M = -5.6 and SD

= 7.5) and late-onset (M =-2.2 and SD = 7.3) scores for "Executive Function" fell within the

Extremely Low range (Severely Impaired) with no significant difference between the two

groups. Mean scores for the remaining neuropsychological tests, including IQ, fell within

the average to below-average range of functioning.

Psychosocial data

Significant differences were observed between groups for "Childhood Physical

Abuse" ($\chi2$ (1, *N*= 37) = 9.9; *p* <.005) with child abuse being more frequently observed in

conjunction with childhood-onset CD [Childhood-onset: 12 (67%); Adolescent-onset: 3

(16%)]. There were no significant differences for "Current Living Arrangements – living in

a single parent household" ($\chi2$ (3, *N* = 42) = 7.1; *p* = .06), "Household Mental Illness" ($\chi2$

(2, *N* = 43) = 1.2; *p*= .55), "Household Learning Disability" (χ2 (2, *N* = 43)* = 2.1; *p*= .35)

and "Household SUDS" ((χ2 (2, *N* = 43) = 1.6; *p* =.45).

Table 1.2. Means, standard deviations and effect sizes for neuropsychological and

psychiatric measures and psychosocial risk factors. Odds ratios and confidence intervals at

95% for nominal data.

	CO CD (M ± SD) Childhood onset	AO CD (M ± SD) Adolescent onset	Cohen's d
PSYCHIATRIC MEASURES			
BPRS total	38.7 ± 9.87	31.7 ± 6.64	.83
ADHD	16 (70%)	13 (65%)	
	r= 0.6; 0.4 + 0.7	*r*= 0.5; 0.3 + 0.7	
YMRS	6.36 ± 9.2	0.7 ± 1.9	.85
HAMD	7.0 ± 5.3	4.8± 4.9	.43
Kessler-10	19.8 ± 5.6	20.8 ± 8.3	.14
DASS depression	9.6 ± 11.1	9.1 ± 9.9	.04
DASS anxiety	7.1 ± 6.4	5.7 ± 6.4	.22
DASS stress	13.5 ± 10.4	10.8 ± 11.3	.25
Severity of CD	14 (77.8%)	4 (22.2%)	
	r= 0.6; 0.3 + 0.8	*r*= 0.3; 0.006 +0.5	
Severity of Primary Drug Dependence	12 (66.7%)	6 (33.3%)	
	r= 0.5; 0.2 + 0.7	*r*= 0.4; 0.07 + 0.6	

NEURO-

PSYCHOLOGICAL

DATA

Head Injury	9 (69.2%)	4 (30.8%)	
	$r= 0.5; 0.2 + 0.7$	$r= 0.3; 0.06 + 0.5$	
RAVLT composite	-3.13 ± 3.23	0.18 ± 3.35	1.00
Spatial Span	-0.68 ± .81	0.10 ± 1.10	.81
Executive function composite	-5.6 ± 7.5	-2.2 ± 7.3	0.5

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Childhood Abuse	12 (67%)	3 (16%)	
	$r= 0.5; 0.2 + 0.7$	$r= 0.3: -0.03 + 0.5$	
Contact with law enforcement	18 (78%)	8 (40%)	
	$r= 0.6; 0.4 + 0.8$	$r= 0.4; 0.1 + 0.6$	
Household dysfunction composite	4.6 ± 0.93	5.1 ± 1.2	0.5

BPRS: Brief Psychiatric Rating Scale; ADHD; YMRS: Young Mania Rating Scale; K-10:

Kessler-10; DASS: Depression Anxiety Stress Scale; RAVLT: Auditory Verbal Learning

and Memory composite.

Discriminant Function Analysis

Results are presented in more familiar form of multiple regression for ease in

interpretation and because raw B coefficients are on the scales of the predicted variables.

Table 1.3 shows verbal learning and memory (RAVLT) composite, executive function

composite, BPRS Total, internalizing symptoms composite, childhood physical abuse and

household dysfunction composite predicting onset of antisocial behavior.

Table 1.3 Discriminant Function Analysis of Neuropsychological, Psychiatric and Psychosocial variables

Variable	Unstandardized Coefficients		β	t	p
	B	SE B			
RAVLT	.06	.03	.41	2.1	.04
Executive Function	-.01	.01	-.07	-.36	.72
BPRS Total Score	-.01	.01	-.20	-1.3	.20
Childhood physical abuse	.39	.14	.38	2.7	.02
Household dysfunction	.05	.08	.10	.59	.55

Note. R^2 = .50 (N=27, p<.05)

Two predictors (RAVLT composite and childhood physical abuse) contributed significantly to the model of onset of antisocial behavior (see Table 3 for unstandardized coefficients for each significant predictor), a finding that accounted for 50% of between group variance ($\underline{R}^2$ =.50, adjusted $\underline{R}^2$ = .34, F(6, 20)=3.3, $p<.05$). Childhood physical abuse (β = .42, <.05) and auditory verbal learning and memory (β = 41, <.05) significantly weighted the discriminant analysis between early and late onset antisocial youth and were the best predictors for distinguishing between the two groups. The early onset CD group were more likely to have auditory verbal learning and memory deficits and experience childhood physical abuse than late onset CD, independent of other predictor variables. However the analysis did not discriminate between the two groups for BPRS Total Score (β

= -.19, n.s.), executive function ((β = -.07, n.s.) and household dysfunction (β = .10, n.s.). Thus, early and late onset CD differed most notably on neuropsychological deficits related to auditory verbal learning and memory processing as well as their reported experience of childhood physical abuse. The two groups did not differ on depression and anxiety symptoms, with both groups reporting low levels of these symptoms. Nor, did they differ on positive psychiatric symptoms independent of other predictors, although the early onset CD reported 'moderate' levels of positive symptoms with the late onset CD reporting 'minimal' symptoms on average. Both groups had the same degree of family dysfunction, based on self-report of family substance use, incidence of mental illness and physical/learning disability.

DISCUSSION

The current study examined psychiatric, neuropsychological and psychosocial risk factors in distinguishing childhood- from adolescent-onset CD. Childhood-onset conduct disorder was characterized by: (1) impairment of verbal learning and memory (as indicated by the RAVLT); (2) higher reporting of childhood physical abuse; (3) higher rates of mental-health problems, specifically psychotic-like symptoms, but not depression and anxiety; (4) lower levels of education; (5) more contact with police and juvenile justice agencies; and (6) committing more serious, violent offences. All findings were associated with large effect sizes.

Childhood-onset CD youths displayed global cognitive impairment across executive function, verbal learning and memory. They were significantly more likely to suffer from neuropsychological deficits measured by the RAVLT, a finding associated with a large

effect size. The RAVLT evaluates verbal learning, memory and auditory processing, and includes functions such as proactive inhibition, retroactive inhibition, retention, encoding versus retrieval and subjective organization [55]. Performance IQ was observed to be greater than Verbal IQ in a number of delinquency studies suggests childhood onset CD youth may suffer from a specific deficit in language manipulation. This was a strong discriminator between groups in our study with childhood onset CD showing substantial impairment in the language-based measures. Verbal deficits affect receptive listening and reading, problem solving, expressive speech, writing and memory for verbal material [66] and it has been suggested that verbal ability is a necessary skill for self-control of behavior, as it influences the success of socialization, beginning with parent-child interactions [7], [8]. Our results support previous findings as subjects performed poorly in language-based neuropsychological tests and memory tests, but not in non-language-based tests. Our study provides an important contribution as it focused on a more homogeneous CD group, rather than relying on a delinquency cohort.

Both childhood- and adolescent-onset groups were in the "severely impaired" range for executive functioning. Both verbal and executive-function deficits are likely to contribute to the antisocial behavior in these groups, reducing the child's ability to control their own behavior and therefore act out impulsively. These results suggest a shared vulnerability, with dimensional differences in brain development related to executive function between the two groups. Any degree of impairment with cognitive function is likely to place a young person at risk of impulsive behavior and poor decision-making. Our results suggest that adolescent-onset CD may not be a normative process, as the adolescent-onset sub-group also displays impairment in executive function. This is consistent with previous studies [28]–[30] showing similar neurophysiological profiles in both childhood-

and adolescent-onset CD. What distinguished the two groups in our study was language-based performance.

Both childhood- and adolescent-onset groups reported moderate to severe depression, anxiety and stress symptoms on a range of depression and anxiety measures, with no significant differences between the two groups. Childhood-onset youth had a significantly higher mean score on the Young Mania Rating Scale and the Brief Psychiatric Rating Scale than the adolescent-onset youth, although they fell below the symptom threshold for both measures. Three subjects (two childhood-onset and one adolescent-onset) who reported psychotic symptoms at the time of interview, had previously used cannabis or hallucinogens and it was suspected that in these cases, psychotic symptoms were substance induced, with symptoms remaining following the cessation of substance use. Research suggests higher rates of psychotic illnesses amongst adult and juvenile offenders [148]-[151], [68], however few studies have examined differential rates of mental health problems between early and late onset conduct disorder. Psychiatric symptoms, particularly first episode psychosis have been linked with violent behaviour in a number of studies [152]-[153], [13], [67], [68]. Symptoms that were more frequently reported by early onset CD include; mania, suspiciousness, perceptual disturbance, unusual thought content and bizarre behaviour and confusion. Although mean scores were sub-clinical, this study provides some support for fluctuating mood and psychosis emerging in early onset youth.

Psychosocial risk factors can significantly impact and increase the risk of developing chronic conduct problems. Parental antisocial personality disorder, alcohol dependence, mood disorders and schizophrenia have been found to be higher for childhood-onset CD.

Findings from our study did not indicate significant differences between groups for family risk factors, although childhood-onset youths were more likely to have experienced childhood physical abuse than their adolescent-onset peers, a finding associated with a large effect size. Childhood-onset youths also reported significantly fewer years at school. It was anticipated that early-onset youths would have higher rates of substance use than adolescent-onset youths, however, the Severity of Dependence Primary Drug scale did not demonstrate differences between the two groups. This could be due to legal issues related to reporting or abstaining from substance use whilst a young person is under a community treatment order or parole conditions. Childhood-onset youths were also more likely to have contact with police and juvenile justice agencies as well as committing more serious, violent crimes. Overall, there was a relationship between auditory verbal learning and memory, child abuse and childhood-onset CD independent of other risk factors.

The strengths of the study include a sample population of CD youth distinguishing for age of onset based on the presence of behavioral difficulties. This reduces the heterogeneity usually associated with measuring risk factors in antisocial youth populations, a significant strength of our study. Previous studies have focused on delinquent populations in custody rather than community settings. Few studies have examined subjects with a diagnosis of conduct disorder. There are important distinctions between the two groups, as conduct disorder refers to a mental disorder and juvenile delinquency to a legal status. Juvenile delinquency is more prevalent than conduct disorder. A designation of juvenile delinquency only requires participation in one illegal act [69]. Time of onset for delinquency groups is, therefore, arbitrarily based on criminal charges rather than the onset of antisocial behavior. Focusing on the diagnosis of conduct disorder however – as we do here - provides a more homogeneous group for study. Furthermore, delinquency research has not always

accounted for comorbidity, with dual diagnoses of conduct disorder and ADHD resulting in the poorest outcomes and strongest predictors of adult crime [7]. In the current study, there were no significant differences for ADHD between the two groups, suggesting that observed differences were related to age of onset of CD rather than the presence/absence of ADHD.

The limitations of the study include a relatively small sample size, measures of substance use that do not reflect usage at the time an offence was committed and demographic measures based on self-report. Collaborative information regarding a subject's family history would allow for better discrimination of these factors in future studies. The two sample groups were also overwhelmingly male, an observation that is representative of the CD population [70]. Additionally, information on ethnicity and socioeconomic status was not consistently recorded for participants. Finally, it is noted that testing occurred prior to the publication of DSM-5, therefore we did not assess participants on capacity for prosocial emotions, which is now a specifier for conduct disorder diagnosis in DSM-5. This specifier may help to identify characterized by callous-unemotional traits.

In conclusion, our study reveals that childhood- and adolescent-onset CD differed for a number of psychiatric, neuropsychological and demographic risk factors. Childhood-onset CD performed more poorly than adolescent-onset CD for auditory verbal learning and memory tasks, but did not differ for measures of executive function. Both groups exhibited severe impairment on executive function tasks challenging theory indicating that adolescent-onset-CD may be a normative process. Childhood-onset CD also exhibited more psychotic-like symptoms than adolescent-onset CD. Those with childhood-onset CD reported child abuse more frequently. Childhood-onset youths had more frequent contact with juvenile

justice agencies and they committed more serious acts of violence. This study is unique as it integrates risk factors across psychiatric, neuropsychological and psychosocial domains of function in a CD population, distinguishing for both the time of onset of CD as well as comorbid ADHD. Further investigations into CD subtypes, such as CD and comorbid ADHD and CD alone, are necessary to distinguish unique risk factors amongst sub-groups. Children with ADHD are more likely to receive a comorbid diagnosis of oppositional defiant disorder and conduct disorder and they are more likely to have written language disorders and executive function deficits [71]. The two groups in the present study did not differ in rates of ADHD and were therefore controlled for, however the small number of subjects in the subgroups limited the power of the analysis.

In conclusion, our findings provide support for Moffit's dual taxonomy model in that childhood-onset youth were found to exhibit vulnerabilities across multiple risk factors. Children with deficits in verbal skills and executive function who are experiencing physical trauma and childhood abuse are more likely to experience behavioral problems that set the stage for developing violent and antisocial behavior. However, our findings also challenge Moffit's "normative" theory of adolescent onset antisocial behavior providing support for Fairchild's [29] developmental theory. Our findings highlight the need for further investigation in larger samples.

CHAPTER 2

Externalizing versus Internalizing Disorders in Young People: Focus on Neuropsychological and Psychosocial Function

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Abstract

Objective: Problem behaviours emerging in childhood and adolescence may be explained by two psychiatric dimensions of internalization and externalization. Few studies have measured neuropsychological dysfunction extensively across the two domains. This present study investigates whether young people with externalizing problems have higher rates of neuropsychological and psychosocial dysfunction than young people with internalizing problems.

Method: One-hundred and forty-eight adolescent participants (81 males, 67 females, mean age = 14.5, age range 12-16) with a diagnosis of either an externalizing disorder (n=32), internalizing disorder (n=80) or comorbid externalizing/internalizing disorder (n=36) were recruited through Headspace Services. Participants completed a battery of psychiatric, neuropsychological and psychosocial measures. Neuropsychological function was also compared to normative scores.

Results: All three psychiatric groups showed impairments on executive function measures, with significant differences between the groups $F(2,132) = 4.9$, $MS = 125$, $p = .009$. The externalizing group performed significantly worse than both the internalizing and comorbid groups.

Conclusion: The externalizing group displayed greater cognitive impairment, and more severe executive deficits in particular, than both the internalizing and comorbid groups. Findings provide support for a dimensional symptom-based approach in understanding psychopathology and the potential of neuropsychological deficits to underlie this.

Key words: externalizing disorders, internalizing disorders, neuropsychology, psychiatric illness

INTRODUCTION

Research into childhood and adolescent psychiatric disorders has frequently identified two higher order factors of comorbidity among individual mental health disorders internalization and externalization. Internalizing disorders are characterized by mood and anxiety disorders and externalizing disorders are typified by substance use disorders, delinquency and anti-social disorders [76], [154]. While these studies indicate high rates of co-occurrence of mental disorders within the domains of externalizing and internalizing disorders, emerging evidence suggests that there are also high rates of comorbidity between the externalizing and internalizing domains. Previous research has investigated developmental progression of externalizing behaviours in childhood and adolescence and their relationship to the development of internalizing disorders in pathways analyses (see 111 for a review), through factor analytic studies [76], [91] and cross-sectional analysis [155], [156]. Other studies have shown developmental sequences of internalizing and externalizing problems in adolescence and often co-occur at greater than chance rates [157], [17] with externalizing problems decreasing and internalizing problems increasing with age and high comorbidity across domains [158] which may be suggestive of a general underlying vulnerability within these domains.

Most research has focused on either single disorders or single domains [158], leading to gaps in understanding of changes in one domain and how it relates to changes in another. Research into developmental pathways has been less than uniform with large numbers of possible developmental sequences, with different methods of investigation and identification of onset of behaviours. A large body of cross-sectional findings suggests that externalizing and internalizing problems often co-occur and change together over time [159] − [162]. Patterson et al's [164] failure model argues that conduct problems often antecede

internalizing problems as failures in social situations gradually lead to depression and anxiety. In Capaldi's [165] study, boys with conduct problems in Grade 6 predicted depressive symptoms in Grade 8.

Few studies have compared the neuropsychological impairments associated with these domains. Neuropsychological research of antisocial behaviour has found evidence of verbal/language deficits, memory difficulties and executive dysfunction [176]. Extensive evidence of neuropsychological deficits, particularly executive function (EF) deficits has been cited in the attention deficit hyperactivity disorder (ADHD) literature. A path of early and persistent neuropsychological dysfunction and aggression was identified by Moffitt [177] and replicated by others [176], [178]. Similarly within the internalizing disorders, high co-morbidity has led to a poor understanding of distinguishing neuropsychological features, however, deficits in executive function, memory, attention and concentration, and processing speed have been associated with both depression and anxiety in young adults [109]. We argue that by using underlying categories of internalizing and externalizing and grouping reported disorders into these underlying categories, important insights may be gained into brain-behaviour relationships.

Developmental pathways in externalizing problems

Externalizing disorders typically involve problems in controlling behaviour due to poor impulse control and acting out. Disorders classified as externalizing include oppositional defiant disorder (ODD); conduct disorders (CD) and ADHD. High rates of comorbidity among the "externalizing disorders" have been demonstrated through epidemiological studies and account for more than half of the childhood referrals to mental health clinics [166], [85-89] with co-occurrence between ADHD, ODD and CD between

29% and 71% of the time in large epidemiological studies and clinical studies [84].. Other large-scale community samples have found comorbidity rates between the externalizing disorders range up to 90% [81] - [83].

Similar risk factors have been indicated for juvenile externalizing disorders with high sensation seeking, low avoidance of dangerous situations and a history of disruptive family environments [167]. Some studies have suggested that a common vulnerability exists between the hyperactive and antisocial behavior and that multiple disorders are more severe than single disorders [168]. Retrospective data from a national survey of adults [169] reported that the onset of ODD usually precedes the onset of CD. The onset of ODD is typically later than the emergence of ADHD when the disorders co-occur in the same individual. ADHD has been found to be comorbid with ODD and CD [157], [170] and is considered a strong risk factor for CD [171], [83] with the onset of CD being particularly early, prior to age 12, in boys with ADHD [172], [173]. There is some evidence in more recent work, for a progression from ADHD to ODD followed by CD and depression [174]. The developmental relationship between ADHD and other disruptive behaviour disorders (DBD) is not entirely clear, but has historically been regarded as a strong risk factor for CD [111], with a direct relationship theorized by many researchers [171]. While externalizing disorders are far more common in boys [179] girls exhibiting externalizing behaviours display similar patterns to boys [175].

Developmental pathways in internalizing disorders

Internalizing symptoms as measured on the Child Behaviour Checklist (CBCL) [74] encompass symptoms of anxiety, depression and withdrawal and children with internalizing scores displaying excessive sadness, fear, anxiety, depressive affect and social withdrawal

[75]. The internalizing disorders, comprising mood and anxiety problems are among the most common forms of mental illness in both adolescence and adulthood. Twelve-month prevalence of major depressive disorder in the United States is approximately 7% with a threefold increase in young people between 18 to 29 years [180]. Twelve-month prevalence of generalized anxiety disorder is 0.9% among adolescents and 2.9% among adults in the general community of the United States [181] There is considerable overlap among the internalizing disorders and substantial comorbidity has been found among the mood and anxiety disorders across the lifespan [90]. Females are more likely to have an anxiety disorder in childhood, however gender is less likely to predict anxiety in adolescence [182].

Comorbidity between internalizing and externalizing problems

Some studies suggest co-occurrence between the externalizing and internalizing dimensions, although the results differ with regard to the strength of associations [157], [183], [16], [17]. Some researchers have queried whether differences in findings are related to samples studied as clinically referred adolescents may show more co-occurrence between externalizing and internalizing problems than adolescents from the general population because young people with multiple disorders are more likely to seek help than young people with single disorders [91]. While rates of co-occurrence within dimensions are higher, individuals with an externalizing disorder are at a higher risk of being diagnosed with an internalizing disorder and vice versa. This suggests that there may be common factors that predispose individuals to externalizing and internalizing disorders.

The neuropsychology of externalizing disorders

An abundance of studies have documented evidence of frontal lobe dysfunction and executive dysfunction in childhood and adolescence with ADHD [92-98] and have linked

these deficits to behavioural symptoms of impulsivity, inattention and hyperactivity [184].

For example, adolescents with ADHD show impairments on response inhibition and

processing speed tasks and increased response time variability [185], [187].   Executive

function deficits have also been linked with antisocial behaviour in various studies [99-105].

Earlier reviews of the delinquency literature by Moffitt [6], identified deficits in three areas:

executive function, language abilities and cerebral dominance. The literature linking

language and behavioural maladjustment at various developmental periods from childhood

to adolescence is consistent and convergent [186] – [193].   Rates of language deficits in

children identified with disruptive behaviours range between 24% to 65% [194] and

disruptive behaviours found in children identified with language delays range from 59% to

80% [187], [195]. Most research has been descriptive or correlational with measurement of

individual cognitive functions rather than simultaneous measurement across cognitive

function.   However a study by Sequin and colleagues [106], using a broad range of

neuropsychological measures to assess cognitive function, found working memory

impairment, even after excluding executive function, in a community sample of boys with a

history of physical aggression.

The neuropsychology of internalizing disorders

Studies investigating differences between the two broad-band classifications of

internalizing and externalizing disorders as measured on the CBCL [159], found that

internalizers were more likely to have higher Verbal and Full Scale IQs than externalizers,

however, there were no differences on Performance IQ or overall achievement between the

two broad-band groups [107].

Depression has been associated with reduced functioning in attention, concentration,

working memory in both verbal and visual tasks and processing speed. However, evidence

suggests that after an episode of depression resolves, cognitive function returns to premorbid levels [108]. Neuropsychological findings for children and adolescents with anxiety disorders have been less consistent, and often depend on the subtype of the anxiety disorder as well as severity [179]. OCD has been found to be associated with deficits in executive function, visual memory, attention and processing speed in young adults [109-110]. Overanxious children were found to have poorer performance on a word-learning task, but no differences were found on visual-motor reproduction and memory tasks [110].

Aims of current study:

The aim of the current study was to examine the interrelationship between internalizing and externalizing disorders through the assessment of neuropsychological deficits and psychosocial impairment and examine whether common or distinct neuropsychological factors underpin each domain. We hypothesize that the externalizing group will exhibit a more severe neurocognitive dysfunction particularly within the area of executive function, as indicated in the literature. Less is known about the neuropsychological profiles of young people with a comorbid externalizing/internalizing disorder. The literature has also been less clear about neuropsychological function in the internalizing disorders, as neurocognitive deficits may be transient and episodic; therefore we anticipate neuropsychological deficits to be less severe.

This study will therefore focus on the neuropsychological and psychosocial function of youth with externalizing, internalizing and comorbid externalizing/internalizing disorders and addresses the following hypotheses:

1. Externalizing disordered youth will show more severe neuropsychological deficits, including verbal learning and memory and executive function deficits when compared with the internalizing disordered and comorbid groups.

2. Internalizing disordered youth are expected to have moderate impairment in verbal learning and memory and executive function when compared with the externalizing groups and a normative sample.

3. Internalizing disordered youth will display moderate impairment in attention and concentration, visual and verbal working memory and processing speed deficits when compared with age related norms.

4. Externalizing disordered youth will have higher rates of psychosocial dysfunction compared to the internalizing disordered and comorbid groups.

As late adolescence, 16 years and over, signifies the emergence of more serious mental health problems such as psychotic illnesses and bipolar spectrum disorders, we have focused on young people within the age range of 12 to 16 years to examine both the neuropsychology and comorbidity between internalizing and externalizing disorders as it is anticipated that a clearer distinction between these two dimensions will be observed at this stage of adolescent development.

METHOD

Participants

One hundred and forty eight young people (age range: 12-16 years, M: 14.5, SD: 1.3; gender: M: 81, F: 67) diagnosed with either an internalizing, externalizing disorder or comorbid internalizing and externalizing disorders were recruited for this study through the

Headspace services – a group specializing in the assessment and early intervention of mental health problems in young people 942], [43].   Inclusion criteria were (i) persons aged between the ages of 12 and 16 years and (ii) met DSM-IV-TR criteria for a diagnosis of either an externalizing disorder, internalizing disorder or comorbid externalizing and internalizing disorder.   Exclusion criteria were (i) psychotic illnesses and (ii) bipolar spectrum disorders, which were generally met by limiting the cut-off age at 16 years, before the emergence of more serious disorders and to detect disorders as they emerge.   Participants failing to meet criteria for a diagnosis on either of the two dimensions were excluded from the study.

Ethics statement

This study protocol was approved by the Human Research Ethics Committee at The University of Sydney (Ref No. 02-2009/11107). Participants were informed, via a "Participant Information Statement" that participation is entirely voluntary, and if they agree to participate, they may withdraw consent at any phase of the study without prejudice. As all participants were between the ages of 12 to 16 years, parents or guardians were required to give written consent via the "Parental (or Guardian) Consent Form" alongside consent of the child.   Participants and their legal guardians were informed of limits of confidentiality regarding offending behavior, via the information sheet provided, as well as a script read aloud to participants prior to the commencement of the clinical interview. All participants under the Juvenile Justice System were accompanied by a caseworker, who provided additional information regarding a participant's capacity to consent. If mental health problems were identified during the assessment process for a participant, they were offered information regarding treatment or referred to a mental-health clinician at Headspace Services, Camperdown.

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Procedure

Psychiatric symptoms, neuropsychological deficits and psychosocial risk factors were determined using a variety of measures, which are described below. A psychiatrist or clinical psychologist conducted clinical interviews for all potential participants, and a diagnosis of ODD/CD, ODD/CD and ADHD or ADHD alone (externalizing disorder) was given if DSM-IV-TR criteria for the disorders were met. A diagnosis of depression or anxiety (internalizing disorder) was given if DSM-IV-TR criteria for the disorders were met. An absence of any criteria characteristic of an externalizing disorder was required to meet criteria for an internalizing disorder. An absence of any criteria characteristic of an internalizing disorder was required for inclusion in the externalizing group. These decisions were based on clinical interview and made by the referring clinician. Participants that met criteria for both an internalizing and externalizing disorder were recruited to the comorbid group. Approximately six experienced psychiatrists and clinical psychologists working out of the Headspace clinic were responsible for making the diagnoses. Clinicians attend regular meetings to discuss cases and protocols to ensure inter-individual reliability and validity of diagnoses. Once participants were referred to the study, a research psychologist re-assessed their diagnosis. In general, the research psychologist's assessment of diagnosis concurred with the referring clinician. Discrepancies were noted within the database for the participant in question.

Psychiatric Measures

Kessler Psychological Distress Scale-10

The Kessler psychological distress scale (*K-10)* [45] is a widely used, simple self-report measure of psychological distress consisting of 10 items and scored using a five-level

response scale based on the frequency of symptoms reported for each question. It is useful in the identification of individuals who need further assessment for anxiety and depression. *Reliability and Validity:* The scale has good construct and criterion validity [118], showing strong association with mental health symptom measures as well as frequency of consultations for mental health problems in a 12-month period [119]. Kessler et al [118] found high levels of sensitivity and specificity with high Cronbach's alpha (.93). The K-10 was hand scored by research psychologists.

Depression Anxiety Stress Scale 21

The Depression Anxiety Stress Scale 21 (DASS) [46] is a valid and reliable measure of depression, anxiety and stress separately [47]. Each of the three DASS-21 scales contains seven items, divided into subscales with similar content. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale is sensitive to levels of chronic non-specific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. Scores for depression, anxiety and stress are calculated by summing the scores for the relevant items. The DASS-21 was administered to determine mild/moderate/severe/extremely severe scores for each DASS scale. *Reliabilty and Validity:* The DASS-42 has excellent internal consistency and test-retest reliability and can distinguish between features of depression, physical arousal and psychological tension and agitation better than other existing measures [120], [119], [46]. This was confirmed in later studies and extended to apply to the DASS-21 [121], [119]. Cronbach's alphas for the DASS-21 subscales were 94 for Depression, .87 for Anxiety and .91 for Stress.

Hamilton Depression Rating Scale

Hamilton Depression Rating Scale (HAM-D) is a clinician-administered rating scale to assess symptom severity in depressive disorders. Symptoms are rated on a severity scale in individuals otherwise diagnosed with depression. It is a questionnaire used to provide an indication of depression and as a guide to evaluate recovery. Although the HAM-D form lists 21 items, the scoring is based on the first 17 items. Eight items are scored on a 5-point scale, ranging from 0 = not present to 4 = severe. Nine are scored from 0–2. A score of 0–7 is considered to be normal. Scores of 16 or higher indicate full symptomatic status [41]. *Reliability and Validity:* Trajkovic [122] found a pooled mean for alpha coefficients in random effects model was 0.789 (95%CI 0.766-0.810) suggestive of good levels of internal consistency. Inter-rater reliability, pooled means in random effects model were 0.937 (95%CI 0.914-0.954) for the intraclass correlation coefficient, 0.81 (95%CI 0.72-0.88) for the kappa coefficient, 0.94 (95% CI 0.90-0.97) for the Pearson correlation coefficient, and 0.91 (95%CI 0.78-0.96) for the Spearman rank correlation coefficient. Test-retest reliability ranged between 0.65 and 0.98 and generally decreased with extending the interval between two measurements. These results suggest that the HAM-D provides a reliable assessment of depression. The HAM-D showed adequate convergent validity in correlations with all but two scales, including the major depression section of the Structured Clinical Interview for DSM-IV [123]. Discriminant validity: Zheng et al [123] reported that the HAM-D was able to discriminate psychiatric patients classified as mildly, moderately and severely dysfunctional.

Brief Psychiatric Rating Scale

The Brief Psychiatric Rating Scale (BPRS) [48] is a 24-item scale for the identification and quantification of psychiatric symptoms. The instrument contains 24 ordered category-rating scales to assess positive and negative symptomatology in discrete symptom areas. The BPRS is a sensitive and effective measure both of psychopathology and of treatment-related symptom changes (Hedlund and Vieweg, 1980, as cited in [49]). Suggested cut-off scores for the BPRS have usually related to the total score rather than subscales. A range of 31 to 40 relates to a "minimally ill" level of psychological distress; 41 to 53 relates to "moderately ill"; and above 53 is considered "markedly ill" level of psychological distress [49]. The BPRS Total score will therefore be used to determine cut-offs for the two groups. A review of published studies of the BPRS reported interrater reliability for the total pathology score at 0.80 or greater for 10 out of 13 studies. The median reported Pearson correlation for individual items ranged from 0.63 to 0.83 in 5 studies [216]. The reported validity of the BPRS is generally high when compared with other measures of general psychopathology [217].

Neuropsychological Measures

Trained research psychologists administered a battery of neuropsychological tests covering a number of cognitive domains including Intellectual Ability, General Knowledge, Processing Speed, Simple Attention, Sustained Attention, Working Memory, Learning & Memory – Verbal, Learning & Memory – Visual, Visual Spatial, Executive Functioning, Cognitive Flexibility, Executive Functioning – Verbal Fluency. Measures were combined into composites if they measured similar areas of cognitive functioning. Test scores were converted to z-scores to ensure common means and standard deviations and then summed and averaged. All the tests had recent norms that are representative of the age and

educational status for the population under investigation. All the instruments were well standardized, reliable and validated in prior studies. The test battery was designed to assess: intellectual ability, speed of information processing, working memory, executive function, planning and organization, simple and sustained attention, visual spatial skills, visual and verbal learning and memory and processing speed.

Wider Range Achievement Test R

The Wider Range Achievement Test R (WRAT-R) [53] is the child version of academic achievement, administered to participants 16 years and younger. It consists of a word reading list and estimates IQ. It has been co-normed with the third editions of the Wechsler Adult Intelligence and Memory Scales. The word pronunciation format of the test is identical that of the National Adult Reading Test-Revised (NART-R) [126]. Use of the WRAT-R Reading for premorbid prediction compares favorably to regression-based procedures [126].

Wechsler Intelligence Scale for Children-III (WISC-III)

The *Wechsler Intelligence Scale for Children-III (WISC-III) Information* was administered to participants, 16 years and younger. *Information i*s a subscale of the verbal IQ score and is a measure of general knowledge. *Validity and Reliability:* Average reliability coefficients for the WAIS-III are high for most of the individual subtests and range from .93 to .70. Internal consistency figures for Information range from .89 to .93 across age groups. Average stability coefficients for Information are excellent [126]. Inter-rater reliability is reported to be high (>.90) [126]. There is substantial correlation (.80 and above) between the WAIS-III and its predecessors.

Trail-Making Test

The Trail-Making Test (TMT) is a measure of attention, speed and mental flexibility. It consists of parts A and B. Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1–25, and the patient is required to draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A–L); as in Part A, the participant draws lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1–A–2–B–3–C, etc.). The participant should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Part B of the TMT has been found to be the most sensitive to frontal damage and involves the ability to alternate between, and maintain, two sets of stimuli [54]. *Reliability and Validity:* Dikemen [127] found coefficients were adequate for Part A (.79) and high for Part B (.89). Levine et al [128] also found adequate coefficients (.70 for A and B). Inter-rater reliability has been reported as .94 for Part A and .90 for Part B. Good validity had been reported in terms of the TMT's sensitivity to neurocognitive deficits and localized brain dysfunction, particularly frontal lobe abnormalities [129]-[130].

Controlled Oral Word Association Test

Controlled Oral Word Association Test, abbreviated COWA or COWAT, is a verbal fluency test that measures spontaneous production of words belonging to the same category or beginning with some designated letter. The participant is asked to name words beginning with a letter, excluding proper nouns, for one minute and this procedure is repeated three times. The most common letters used are FAS because of their frequency in the English language. The examiner must quickly write down the words provided by the participant on a

piece of paper. Word generation has been found to be a reliable test of left frontal and executive functions [55]. The Controlled Oral Word Association Test [56] evaluates the spontaneous production of words under restricted conditions. *Reliability and Validity:* Tombaugh et al [131] found internal consistency to be high (.83). In healthy adults, test-retest correlations tend to be high, above .70, for short (one week) as well as long (five years) intervals [127]-[128]. Inter-rater reliability is high (.99) [139] and (.98) [139]. The instrument reports good validity [139].

Cambridge Neuropsychological Test Automated Battery

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computer-administered, nonverbal (visually presented) set of tasks developed to examine specific components of cognition. The software comprises one screening test and 12 principal tests from the CANTAB system [57]–[59]. The CANTAB is designed to test different aspects of mental functioning so that a profile of performance can be constructed, including independence of executive measures and memory factors [60]. The CANTAB subtests consist of: spatial span, choice reaction time, rapid visual processing, intra/extra-dimensional shift and paired associated learning. The test scores are computer generated and give a rating from impaired to high average for: simple and sustained attention, visual and verbal learning and memory, working memory, speed of information processing, visual spatial skills and executive function. *Reliability and Validity:* Internal consistency was reported to be adequate to high, ranging from .73 to .95 in a sample of 4- to 12- year old children [134]. Many of the CANTAB measures were found to have poor test re-test reliability [135]. Lowe et al [135] stressed that the tasks may not be poorly defined or ill chosen but rather, excellent tests of executive ability may depend for their sensitivity on their novelty, restricting their use to a single occasion. Robbins [136] examined the factor

structure of some of the CANTAB subtests (Paired Associate Learning, Delayed Matching to Sample, Pattern Recognition, Matching to Sample, Spatial Working memory, Stockings of Cambridge (Tower of London), Spatial Span, Spatial Recognition, Intra/Extradimensional Shift) and found evidence for a six-factor model and found considerable independence among the different executive measures and separation of executive and memory factors.

Verbal memory

Immediate and delayed verbal memory was measured using the Logical Memory subscale of the Wechsler Memory Scale (WMS-III) [61]. Participants were required to recall stories A and B after a 30-minute delay. The examiner records the number of free recall and thematic units. *Validity and Reliability:* Validity studies are strongly positive [137]. However available data provide no statistical support for separate immediate and delayed indices in either normal or clinical samples. The reliability of WMS-III subtests and indices tends to be adequate to high. The median reliability of subtests is .81 and .87 for Indices. Supplemental subtest scores are lower at .77, but still adequate [138]. The majority of the indexes have stability coefficients in the .80s. Logical memory I and II range from .71 to .91 across age groups [139].

Rey Auditory Verbal Learning Test

The Rey Auditory Verbal Learning Test (RAVLT) is a test of memory where the examiner reads a list of 15 concrete nouns. The examinee recalls as many as possible in any order through five administrations and a recognition trial. It allows for the identification of memory impairment and is a measure of verbal memory. *Validity and Reliability:* Vakil & Blachstein [126] identified two basic factors that they interpreted as reflecting acquisition

and retention. Mueller et al. [126] distinguished between short-term memory and long-term latent memory in two heterogeneous clinical samples. Rosenberg et al [141] found the RAVLT performs well in the identification of patients known to be memory impaired by other criteria. The RAVLT correlates moderately with other measures of learning and memory such as the WMS-R Logical Memory and Visual Reproduction subtests [126] and the CVLT [126]. The RAVLT is sensitive to neurological impairment [126], laterality of brain damage [126] and memory deficits in a variety of patient groups [126]. Internal reliability is high, with (coefficient alpha) of the total score at .90 [126]. The test-retest reliability is marginal /adequate over a 1 year period [126]. Practice effects reduce with different RAVLT versions [126].

Psychosocial Measures

Social and Occupational Functioning Assessment Scale

Psychosocial factors were measured on the Social and Occupational Functioning Assessment Scale (SOFAS) and various items on the semi-structured interview. The *SOFAS* is a clinician-administered measure of problems in social, occupational and interpersonal functioning. It measures the frequency of social activities across seven subscales: *withdrawal/social engagement, interpersonal communication, independence-performance, independence-competence, recreation, prosocial and employment/occupation.* It focuses exclusively on the individual's level of social and occupational functioning and is not directly influenced by the overall severity of the individual's psychological symptoms [44]. *Reliability and Validity:* Strong support has been found for the reliability and validity of the SOFAS [142]-[144]. Birchwood et al [142] found high internal reliabilities (coefficient alpha) and strongly differentiated criterion groups with SOFAS scores correlated with the presence of both negative (r = -0.44) and positive (r = -0.46) symptoms based on

assumptions that negative symptoms contribute to deficits in social functioning. Hilsenroth [145] found the SOFAS exhibited very high levels of inter-rater reliability and factor analysis revealed the SOFAS is a good measure of problems in social, occupational and interpersonal functioning.

Severity of Dependence Scale

Participants were also administered the Severity of Dependence Scale (SDS) [62], which is a short, clinician-administered rating scale used to measure the degree of dependence experienced by users of different types of drugs. The SDS contains five items, all of which are explicitly concerned with psychological components of dependence. These items are specifically concerned with impaired control over drug taking and with preoccupation and anxieties about drug use. Higher scores indicate higher levels of dependence. It is primarily a measure of compulsive use, which is a central component of dependence. *Reliability and Validity:* Good internal consistency (ranging from .8 to .9) has been reported across five samples and good test-retest reliability (.89) over a one-day interval in a sample of heroin users [146], [147]. Construct validity is supported by significant correlations with behavioural indices of dependence including dose, frequency and duration of use [147]. One study found only a moderate level of internal consistency for cannabis dependence (alpha = .72) [147]. Item correlations were statistically significant from .45 to .69 (p<.01).

Data and Statistical Analysis

All statistical analyses were performed using SPSS, version 20 (SPSS Inc., Chicago, Illinois, USA). The various psychiatric, neuropsychological and psychosocial variables were

subjected to independent t-test (continuous variables) and chi square (for categorical variables) analyses to determine whether early- and late-onset antisocial youth could be distinguished on specific risk factors identified in the literature. Significant effects were set at $p < .005$ for t tests and chi-square after applying a Bonferroni correction for repeated tests and small cell sizes. Findings were labeled as trends for chi square results if $p < .05$. Participants were excluded from the study at the point of statistical analysis if they were identified as an outlier deemed to be 1.5 times the interquartile range on all neuropsychological measures. All language-based neuropsychological tests were corrected for years of education within standardized scoring calculations and were appropriately normed. Cohen's d effect size statistics were calculated for each pair-wise comparison. Cohen's guidelines [63], [64] identify 0.2, 0.5, and 0.8 as small, medium, and large effects, respectively. Odds ratios were calculated for chi square statistics indicating the degree of association between binary variables. The statistical threshold of 0.05 (two-tailed) was set for all analyses.

Neuropsychological Composites

Composite measure of executive function: A composite measure of variables was created using the SPSS "compute variable" procedure to measure the construct "executive function" across the delinquency group. Three neuropsychological tests, namely Trail Making Test A and B, Intra/Extra Dimensional shift and COWAT animals and letters were included in the composite as they each measure various aspects of executive function [55]. The Trail Making Test A and B measures visuo-motor tracking, divided attention and cognitive flexibility and is sensitive to frontal lobe lesions [50]. Word fluency and the generation of word lists on the Controlled Oral Word Association Test, F-A-S, is a sensitive indication of brain dysfunction, particularly within the frontal area. People with frontal-lobe

lesions have reduced letter and category fluency and therefore deficient retrieval strategies. Intra-extra Dimensional Shift is a test of rule acquisition and reversal. It measures the visual discrimination, attentional set formation maintenance, shifting and flexibility of attention and, therefore, is primarily sensitive to changes in the frontal areas of the brain [65]. Duff et al [195] study found a strong relationship between executive functioning and memory capacities as measured by the COWAT and Trail Making Test A and B and shared more than 50% of variance in their mixed clinical samples of 212 participants.

Composite measure of auditory verbal learning and memory (RAVLT): Comprised items on the Rey Auditory Verbal Learning and Memory test: RAVLT sum, A6 and A7 and produced through the SPSS "compute variable" procedure. A6-A7 measures susceptibility to proactive and retroactive interferences and correlates moderately with measures of immediate recall (Sum A1-A5) [73].

Psychiatric Composite

The BPRS Total score was used as a general measure of psychiatric symptoms.

RESULTS

Participant Characteristics

The *Externalizing Group* consisted of thirty-two young people with CD=2; ADHD=11; and comorbid Ext: ADHD/CD/ODD=19. The *Internalizing Group* consisted of eighty-two young people with depression=62 and anxiety=20. The *Comorbid Externalizing/Internalizing Group* exhibited various combinations of externalizing and internalizing disorders consisting of thirty-six participants (See Table 2).

On the psychiatric measures (see Tables 2 and 3), the internalizing group exhibited severe to very severe anxiety and depressive symptoms and the comorbid group exhibited moderate to very severe anxiety and depressive symptoms. The unexpected level of anxiety and depressive symptoms exhibited by individuals in the externalizing group may have been obscured by levels of externalizing behaviours observed by the clinician at the time of clinical interview. This might reflect a broader issue within the youth mental health system and the failure to detect internalizing symptoms within the externalizing population. None of the three groups exhibited manic symptoms on the YMRS.

Among the 148 young persons (age range: 12-16 years, M: 14.39, SD: 1.3); gender: (M: 81, F: 67), no significant differences for group were found on subject's age at assessment $F(2,145) = 2.72$, $MS = 1.55$, $p = .10$, with the Externalizing group (M: 14.75, SD: 1.1), Internalizing group (M: 14.71, SD: 1.2) and Comorbid externalizing/internalizing group (M: 14.17, SD:1.2). Significant differences were observed between groups for gender, ($\chi2(2, N = 148) = 19.7$; $p = .00$), with more males in the externalizing group (M = 28, F = 4) when compared with both the internalizing (M = 33, F = 47) and comorbid (M = 20, F = 16) group. There were no significant differences for gender between the internalizing group and comorbid groups. Significant differences were observed between groups for onset of psychiatric illness, $F(3, 105) = 7.2$, $MS = 4.23$, $p = .001$ with onset of symptoms occurring earlier for both the externalizing group ($M = 10.4$ and $SD = 3.5$) and comorbid group ($M = 10.4$ and $SD = 3.8$) than the internalizing group ($M = 12.6$ and $SD = 2.1$). There were no differences observed for education at time of measurement $F(2,109) = .89$, $MS = 3.37$, $p = .41$.

Neuropsychological data

Groups differed significantly on the Choice Reaction Time – 5 choice reaction time $F(2,109) = 2.7$, $MS = 3.0$, $p = .006$, (Cohen's d = 0.8); WRAT standard score $F(2,140) = 8.0$, $MS = 1715$, $p = .001$, (Cohen's d = .8); Predicted IQ $F(2,142) = 7$, $MS = 1072$, $p = .001$, (Cohen's d = 1.0); Spatial Span $F(2,138) = MS = 3.5$, $p = .033$ (Cohen's d = 0.6) and Executive Function $F(2,132) = 4.9$, $MS = 125$, $p = .009$ (Cohen's d = 0.6), with the externalizing group performing worse than the internalizing group on these measures. The externalizing group also performed worse on Executive Function when compared with the comorbid group (Cohen's d = 0.7). All had medium to large effect sizes. No significant differences were observed between groups on WISC information $F(2,108) = 1.8$, $MS = 21.3$, $p = .17$, Trail Making Test "A" $F(2,137) = 1.1$, $MS = 1.0$, $p = .34$, Choice Reaction Time – simple movement time $F(2,104) = .42$, $MS = .31$, $p = .66$, - simple reaction time $F(2,104) = 2.7$, $MS = 1.6$, $p = .08$, - 5 choice movement $F(2,109) = 1.2$, $MS = .71$, $p = .32$, Mental Control or sequences $F(2,102) = 1.3$, $MS = 13.7$, $p = .28$, Rapid Visual Processing A $F(2,135) = 1.9$, $MS = 2.8$, $p = .16$, Rapid Visual Processing B $F(2,127) = 1.1$, $MS = 3.8$, $p = .32$, Rapid Visual Processing mean latency $F(2,127) = .10$, $MS = .21$, $p = .90$, Spatial Span errors $F(2,55) = .26$, $MS = .42$, $p = .78$, Logical Memory, stories 1 $F(2,95) = 2.6$, $MS = 18.4$, $p = .08$, Logical Memory, stories 2 $F(2,94) = .99$, $MS = 6.7$, $p = .38$, , Paired Associate Learning-total errors adjusted $F(2,129) = .15$, $MS = .03$, $p = .86$, Paired Associate Learning – total errors 6 shapes $F(2,128) = .99$, $MS = .18$, $p = .37$, Trail Making Test "B" $F(2,143) = 2.2$, $MS = 5.3$, $p = .12$, Intra/Extra dimensional shift – stages completed $F(2,135) = 2.7$, $MS = 4.0$, $p = .07$, Intra/Extra dimensional shift – errors $F(2,135) = .6$, $MS = .55$, $p = .57$, Controlled Word Association Test – Letters $F2,141) = 2.7$, $MS = 4.8$, $p = .07$, Controlled Word Association Test – Animals $(F(2,141) = 1.6$, $MS = 1.2$, $p = .20$, RAVLT, Auditory Verbal Learning and Memory composite $F(2,145) = .90$, $MS = 11.4$, $p = .41$.

Score interpretation for the WRAT standard score (M = 89.7 and SD = 17.6) for the externalizing group fell within the Low Average (mildly impaired) range while the internalizing and comorbid group fell within the Average range with a significant difference observed for this measure between externalizing and internalizing groups. Although significant differences were found between the externalizing and the internalizing groups for Predicted IQ, all three groups fell within the Average range, with externalizing (M = 92.7 and SD = 14.6), internalizing (M = 102.1 and SD = 11.8) and comorbid (M = 97.1 and SD = 11.8). Significant differences were observed between externalizing and internalizing groups for Choice Reaction Time – 5 choice reaction time with the externalizing disordered group performing worse (M =.21 and SD = .71, Average range) than the internalizing disorder group (M = .77 and SD = .68, High Average range) and the comorbid group (M = .5 and SD = .87, Average range). Significant differences were observed for Spatial Span Length with the externalizing group performing worse (M = -.12 and SD = .81, Average range) than the internalizing group (M = .43 and SD = 1.02, Average) and comorbid group (M = .07 and SD = 1.2, Average range). For the "Executive Function" composite, the externalizing disordered group performed significantly worse than both the internalizing and comorbid groups, falling within the Extremely Low range (Severely Impaired) (M = -4.5 and SD = 5.8) while the internalizing disorder group fell within the Low Average (Mildly Impaired) range (M = -1.1 and SD = 5.1) and the comorbid group performing within the Borderline (Moderately Impaired) range (M = -1.3 and SD = 4.2).

Mean scores for the non-significant remaining neuropsychological tests, including the RAVLT, fell within one standard deviation of the Average range.

Table 2.1.   Means, standard deviations, *p values* and cohen's d for participant characteristics, neuropsychological measures and psychiatric symptoms across externalizing, internalizing and comorbid externalizing/internalizing groups.

	EXT (M ± SD) CD=2; ADHD=11; mixed ext=19	INT (M ± SD) Dep=62; Anx=20	COM(M ± SD) Dep=62; Anx=20	p	Cohen's d
N	32	80	36		
Gender	1.13 ± .34	1.60 ± .50	1.44 ± .50	.00	-1.1 E v I .32 I v C .72 E v C
Age at Assessment	14.75 ± 1.1	14.71 ± 1.3	14.17 ± 1.3	.10	.03 E v I .4 I v C .48 E v C
Years of Education	8.90 ± 1.7	9.00 ± 2.0	8.47 ± 2.01	.41	.05 E v I .26 I v C .23 E v C
Age of onset of Psychiatric illness	10.38 ± 3.5	12.56 ± 2.1	10.4 ± 3.8	.001	.75 E v I .7 I v C .005 I v C
WRAT standard score	.89 ± 17.5	101.8 ± 13.8	95.6 ± 13.5		0.8
Predicted IQ	92.7 ± 14.6	102.2 ± 11.8	97.1 ± 11.8		1.0
Choice Reaction Time – 5 CR	.96 ± .92	1.1 ± .77	.82 ± .64		0.8
Spatial Span Length	-.12 ± .81	.43 ± 1.0	.07 ± 1.2		0.6
Executive Function	-4.5 ± 5.8	-1.1 ± 5.1	-1.3 ± 4.2		0.6 internalizing 0.7 comorbid
HAMD Total	5.43 ± 3.8	11.44 ± 6.4	7.7 ± 5.5		
BPRS Total	34.43 ± 9.0	39.04 ± 10.4	37.4 ± 8.6		

YMRS Total	1.07 ± 1.7	3.6 ± 5.4	3.9 ± 5.8
DASS depression	8.64 ± 9.4	22.5 ± 13.6	13.8 ± 10.9
DASS anxiety	5.5 ± 5.2	15.2 ± 10.1	8.53 ± 6.2
DASS stress	9.3 ± 6.6	22.5 ± 10.6	16.8 ± 10.9
DASS Stress	19.8 ± 5.2	27.8 ± 9.4	21.75 ± 6.1

Gender; Age at assessment; Years of education; Age of onset of psychiatric illness; WRAT-Wide Range Achievement Test; Predicted IQ; Spatial Span Length; Executive Function

Table 2.2. Rating scale descriptions for psychiatric measures

	Normal	Moderate	Severe	Very Severe
HAMD	0-4	5-8	8-11	12-15
BPRS	0-31	32-41	42-52	>53
YMRS	0-6	7-19	>20	
DASS Depression	0-4	5-6	7-10	11+
DASS Anxiety	0-3	4-5	6-7	8+
DASS Stress	0-7	8-9	10-12	13+

[215]

Psychosocial data

There were no significant differences for groups on 'Severity of Dependence-Primary Drug' $F(2,23) = .21$, $MS = 1.0$, $p = .25$, and Social and Occupational Functioning Assessment Scale, SOFAS, $F(2,139) = .21$, $MS = 24.1$, $p = .8$.

Gender differences between groups

Gender was a confounding variable in the study with significant differences found between groups. The externalizing group contained only 4 females to 28 males whereas the comorbid and internalizing groups had a more even male to female ratio. Females were therefore de-selected from the three groups and the analysis on neuropsychological measures repeated to determine whether significant differences were maintained. There were no significant differences for executive function between groups following the second analysis $F(2,70) = 1.7$, $MS = 55$, $p = .19$, even though group means for the internalizing and comorbid groups fell within the moderately impaired range and the externalizing group mean fell within the severely impaired range. Groups remained significantly different for Choice Reaction Time – 5 choice reaction time $F(2,64) = 3.3$, $MS = 1.4$, $p = .043$, Predicted IQ $F(2,77) = 4.4$, $MS = 805$, $p = .015$ and Spatial Span $F(2,73) = MS = 3.8$, $p = .023$.

DISCUSSION

The current study examined neuropsychological and psychosocial risk factors in distinguishing internalizing, comorbid and externalizing disordered youth. Firstly, as expected, the internalizing group showed significant elevation on internalizing symptoms, namely, depressive, anxiety and stress. Interestingly, however, the externalizing condition also showed high levels of anxiety and depression, with reports of moderate to very severe depression, anxiety and stress symptoms. This confirms previous research that shows externalizing disordered youth are at greater risk of developing a comorbid internalizing disorder. It also highlights the difficulties in detecting internalizing symptoms in some externalizing youths, and suggests the use of psychometric testing could more accurately measure mood disturbance in externalizing youths.

In terms of neuropsychological function, significant differences in performance on executive function measures or composite measure were found between all three groups, with the externalizing group exhibiting severe impairment, the comorbid group with moderate impairment and internalizing group displayed mild impairment in executive function. However, when the groups were controlled for gender and females were removed from the study, there were no significant differences between groups. The externalizing group mean remained within the severely impaired range and the internalizing/comorbid group means fell within the moderate range of impairment. Results from the second analysis reflect a reduction in the distance between the means for the three groups. Both analyses found impairments for all three groups on executive function. Our findings suggest that the three groups had difficulty performing EF tasks related to cognitive flexibility and organization. Both results support previous findings that adolescents with externalizing behaviour problems exhibit EF deficits with worse neuropsychological outcomes than comorbid externalizing and internalizing and internalizing groups, when groups contained females. The second analysis may reflect an issue associated with low power. While some have speculated that executive function deficits may causally relate to externalizing disorders, this data might suggest that this could only be the case if the deficits are particularly severe, since mild to moderate deficits are seen across populations.

Executive function, visual memory, attention and processing speed deficits have been found in young adults with anxiety and depressive disorders, particularly OCD and panic disorder [109]. However internalizing disorders are more likely to co-occur with suggestions that anxiety and depression may be two phases of the same underlying pathology [197], [198], with depression more often preceded by anxiety in childhood studies

[199].   Decreases in cognitive functioning, specifically mental flexibility, attention and working memory have been found to be associated with depression in adolescents, however evidence suggests that once an episode of depression resolves cognitive function returns to premorbid levels [108].   Our results did not support previous findings that adolescents with an internalizing disorder exhibit deficits in attention, visual and verbal learning and memory or processing speed. Whilst there were significant differences on some of these measures when compared to the externalizing and comorbid groups, all three groups fell within the average range of functioning.

There were also no significant group differences for auditory verbal learning and memory function, a cognitive domain which can impact on receptive listening and reading, problem solving, expressive speech, writing and memory for verbal material [176, p. 478]. This finding was maintained even after de-selecting females from the sample. All three groups fell within the average range (see Table 1.) for verbal learning and memory function and therefore did not display significant impairment (i.e. Borderline to extremely Low) in this cognitive domain. This result is inconsistent with previous findings, which have shown that verbal memory deficits are associated with delinquent populations, particularly early onset [177], [8].

Both the externalizing and comorbid groups displayed moderate to severe deficits in EF. There may be several reasons for this variation.   Some researchers propose a dimensional approach to understand executive function deficits as children and adolescents with both CD and comorbid ADHD will have more severe symptoms and a worse prognosis in terms of adult antisocial personality disorder than children or adolescents with either

disorder alone [200] – [202].   There is more extensive evidence of EF deficits such as planning, set shifting and response inhibition in ADHD [203] – [205].   Attempting to understand differential deficits in neuropsychological function is made difficult due to high levels of comorbidity between these disorders [203], [205].   Additionally, there are inconsistencies in the literature, with reports that comorbid CD and ADHD results in greater EF deficits than in ADHD alone [206], [82], [207] and that comorbidity between these disorders does not result in more severe EF impairments [203]. Sarkis et al 2005, as cited in [203], Barnett et al 2009, as cited in [203], however grouping these disorders into an externalizing domain can potentially mask or dilute actual differences between disorders.

Other studies have argued that differentiating between these comorbid disorders has the potential of missing complex interactions in cognitive function.   For example, hyperactivity often co-occurs with aggression and can combine in additive ways. Studies examining the neuropsychology of one behavioural dimension, i.e., hyperactivity, inattention, impulsivity, or conduct problem while controlling statistically for the others may be missing important variance relevant to the disorder being examined [208].   In a study examining both these dimensions, Sequin et al [209] assessed young adult males who had a history of physical aggression, based on the CBCL at age 15, as well as a history of hyperactivity and found additive effects for impairments for IQ and working memory. Other studies found strong effect sizes on executive function for criminals and delinquents [201], [211] and poor performance on spatial span, a measure of short-term memory from CANTAB tests, but not on frontal tasks such as Intradimensional/Extradimensional Shift Task, Tower of London, or spatial working memory tasks for incarcerated youths. The externalizing group in our study represented high comorbidity between the externalizing

disorders. Worse performance on executive function measures supports the additive concept.

The internalizing disordered group was found to have high rates of anxiety, depressive and stress symptoms as measured by the Brief Psychiatric Rating Scale (BPRS), the Hamilton Depression Scale (HAMD) and the Depression Anxiety Stress Scale (DASS). The comorbid internalizing/externalizing group reported moderate to severe symptoms of depression, anxiety and stress on the DASS, supporting previous studies, which demonstrated that many young people with conduct problems also show internalizing psychopathology. Evidence linking CD/ODD with depression and anxiety [212] where CD predicts depression, while depression does not predict antisocial behaviour [116], [212] support theories such as the 'failure model' proposed by Capaldi and Patterson [165], [90] which suggests that conduct problems result in failures in social interactions and academic achievement, leading to a lack of support and poor skill development and subsequent depression [165]. An inherent limitation of the current study was the inability to examine the developmental sequence between disorders. As noted by Caspi et al [154], cross sectional design mixes single-episode, one-off cases with recurrent and chronic cases, which differ in severity and possible aetiology of their conditions. However, we did find support for distinctiveness in diagnosis and the developmental sequence of CD predicting depression with onset of an externalizing disorder occurring significantly earlier in childhood than an internalizing disorder. Further research examining disorders longitudinally can assist in understanding the overlap between these domains.

It was anticipated that the externalizing youth would have significantly higher rates of substance use given that substance use disorders have been well documented for this

group [76], however the Severity of Dependence Primary Drug scale did not demonstrate differences between the two groups.   Hermens et al. [213], found frequent use of alcohol, nicotine and cannabis in headspace clients aged between 12 and 17 years, suggesting substance use is problematic in this population.   There were also no differences between externalizing and internalizing youth on the Social and Occupational Functioning Assessment Scale (SOFAS) with both groups reporting some difficulty in social, occupational, or school functioning, but generally functioning well, with some meaningful interpersonal relationships.   Whilst we were unable to determine whether CD/ODD predicts depression, the SOFAS result would seemingly contradict the 'failure model' proposed by Patterson and Capaldi [164] to explain comorbid mood problems in externalizing youth and suggest further pathways research incorporate psychosocial functioning measures.

Strengths of the study include examination of a range of neurocognitive functions and psychopathologies across the domains of internalizing and externalizing disorders, using extensive measures of neuropsychology, psychopathology and psychosocial function.   We examined relationships between manifestations of relevant psychopathology and neuropsychological profiles across the two domains with the intention of improving our understanding of common and distinctive neuropsychological foundations of these disorders.   Previous research has focused mainly on the structure of a range of problem behaviours related to the externalizing disorders in youth.   The present study has focused on both externalizing and internalizing problems and examined whether they can be conceptualized as two separate constructs at the level of psychopathology and underlying neuropsychological deficits.

A number of limitations of the study relate to the data and statistical analyses. The sample was drawn from a clinical population where a wide range of diagnostic categories for youth was represented. While we intentionally limited the age range from 12 to 16 years to provide for a clearer representation of the two domains, we were aware this limited the number of participants with a diagnosis of CD, potentially reducing the effect size on a number of neuropsychological measures. Previous findings have indicated deficits across a number of neuropsychological and psychosocial measures for CD including language deficits. Additionally, we did not assess for differential deficits within the domains for the individual disorders due to the small sample size of some of the disorders. This may have obscured relationships between individual disorders. Previous studies have found that ODD is associated with major depression and anxiety disorders and there are suggestions that ODD may be a prodrome for evolving internalizing disorders [156]. The comorbid group displayed deficits with executive function, although not as severe as the externalizing group, when females were included. Replication of these results with larger samples and controlling for gender, could further explore distinct comorbid conditions as indicated in some studies. This study was cross-sectional and thus, evidence of relationships between the psychiatric dimensions could not be explored. Without longitudinal, prospective data across neuropsychological and psychiatric measures, sequential and causal links between disorders as well as developmental progression of severity remain elusive.

In conclusion and within the context of these limitations, the results of the current study reveal that the internalizing, comorbid and externalizing disordered groups differed in their level of executive function with the externalizing disordered group performing far worse than the other two groups (Cohen's d = 0.6 – internalizing and Cohen's d = 0.7 - comorbid). The groups did not differ across a range of neuropsychological functions, with

all three groups performing within the average range for visual and verbal learning and memory, predicted IQ, attention and processing speed. Not surprisingly the internalizing group exhibited extremely severe levels of depression, anxiety and stress, however the externalizing and comorbid groups also showed moderate to severe levels of depression, anxiety and stress, supporting previous findings of comorbidity between the domains. These findings raise a number of questions regarding the role of EF deficits in the internalizing disorders. Whilst EF deficits have been considered to play a role in antisocial behaviour, there have been varying research findings regarding the association of depression and anxiety with neurocognitive function, with conflicting results in the domains of attention, memory and executive functions [179]. Increased anxiety levels have been shown to produce impairments in attention, working memory and executive function [214], however cognitive dysfunction due to depression and anxiety may be temporary and therefore diminish as symptoms reduce. This study therefore highlights the need for further exploration of distinct trajectories of symptom progression to allow for a comprehensive understanding of functional relationships between psychiatric, neuropsychological and psychosocial dimensions, as well as gender differences in the development of disorders. Longitudinal research in this area, which considers the temporal ordering of distinct patterns of symptoms and comorbidity progression would allow for clarification of disease classification systems which have implications for treatment.

THESIS DISCUSSION

Overall, key findings from these two studies suggest that early onset CD youth were more likely to experience impairment in verbal learning and memory when compared with late onset CD youth and established norms. Both early and late onset CD youth were found to have severe impairment in executive function.   Both CD groups reported mild levels of anxiety and depression, with the early onset group more likely to experience psychotic like symptoms.   Early onset CD youth reported higher rates of childhood physical abuse, involvement in more serious, violent crime and more contact with law enforcement agencies.   In the second study, externalizing disordered youth experienced more severe impairment in executive function than both the comorbid and internalizing disordered youth. However, when females were removed from the study, there were no significant differences between groups, with all three groups showing moderate to severe impairment in executive function. Neuropsychological function in other cognitive domains such as verbal learning and memory were not found to be impaired across groups. The externalizing and comorbid groups reported moderate to severe internalizing symptoms.

The externalizing group also showed earlier age of onset of psychiatric symptoms when compared with the comorbid and internalizing groups. This finding was consistent between studies, as both groups with early onset symptoms, that is, early onset CD and externalizing groups, exhibited more severe neuropsychological dysfunction. The clinical implications of these results are that young people with early onset disorders, presenting to mental health services may benefit from neuropsychological testing as part of the assessment process. Deficits in cognitive function can adversely impact on a young person's ability to perform both academically and socially, which can then potentially exacerbate

their mental health problems. Early detection of neuropsychological deficits can influence treatment options to incorporate skills development strategies in these cognitive areas.

Results from the first study distinguished childhood onset CD youth from adolescent onset CD youth on a range of neuropsychological, psychiatric and psychosocial measures. Childhood onset CD youth displayed global cognitive impairment across executive function and verbal learning and memory, while cognitive impairment for adolescent onset CD youth was only found in the area of executive function. Findings associated with a large effect size and generally consistent with previous studies [8]. Both childhood and adolescent onset youth were 'severely impaired' on executive function. This result was not anticipated; rather, it was expected that adolescent onset youth would display less impairment in cognitive function. However, there are two potential explanations for this unexpected finding. Participants included those diagnosed with CD, a disorder associated with more enduring antisocial behaviours than 'delinquent' participants used in other studies [60], [24], [8]. In contrast to those with CD, 'delinquent' populations may include young people who have engaged in only a few antisocial acts, and the term does not reflect the severity of antisocial behaviour. A second explanation for this unexpected finding is that both early and late onset groups were highly comorbid for ADHD, a disorder associated with severe impairment in executive function. These results do, however support previous research by Fairchild et al [28], [29] and Roisman et al [30], who argue for a revision of the developmental of the antisocial behaviour model as more evidence comes to hand supporting quantitative rather than qualitative differences between the two antisocial subgroups. Our findings challenge the view that adolescent-onset CD is normative, transient in otherwise healthy young people as adolescent-onset participants in our study exhibited moderate to severe deficits in executive function potentially extending into adulthood.

Results from the second study demonstrated significant differences between participants categorized within the internalizing and externalizing domains across a variety of neuropsychological measures. Externalizing youth performed significantly worse (Extremely Low relative to established normative ratings) on executive function than the internalizing and comorbid youth (Low Average to Borderline). Both groups fell within the Average to Low Average range of functioning on these measures. Externalizing and comorbid groups also showed moderate to severe levels of depression and anxiety, suggesting high comorbidity across domains. As gender was identified as a confounding variable, females were de-selected from the sample and the analysis re-run. This second analysis found no significant differences on executive function between groups, however the externalizing group mean remained within the severely impaired range. These results suggest that when internalizing and comorbid females were removed from the study, both internalizing and comorbid males exhibit more impairment in executive function when compared to established norms. Findings of impairment in executive function for internalizing disorders are consistent with previous headspace studies, [213], however gender differences in mood disturbance and associated executive dysfunction were not explored.

The first study supports a theoretical orientation [178], [66] towards understanding conduct disorder, to some degree, based on aetiology, with the earlier the onset of symptoms linked to more severe impairment on cognitive function. Our findings also support Fairchild et al [28, [29] theory that differences between the two groups are quantitative rather than qualitative, as distinct differences between groups were not observed on neuropsychiatric measures, but more typical of a dose-response effect, with environmental factors such as

child abuse, interacting with a longer duration of antisocial behaviour leading to more severe neuropsychological deficits.

Although this study found higher rates of child abuse within early onset group when compared to adolescent onset youths, interactions between cognitive function and environmental risk factors, such as childhood abuse could not be explored due to small sample size. However these results give support to the literature regarding the deleterious effects of child abuse on cognitive function.

Executive dysfunction discriminated externalizers from internalizers in the second study but only when females were included with all three groups showing impairment in executive function. Evidence of global cognitive impairment, including verbal learning and memory deficits for early onset CD youth, found in study one was not found in the second study, with the externalizing group displaying minimal deficits in verbal and learning and memory. This may be due to a number of factors.

1. The study combined youth with different aetiologies.
2. Inclusion of participants with a primary diagnosis of ADHD.
3. Greater variation in severity of symptoms within the wider externalizing group.

It is possible that differences between the domains of externalizing and internalizing may have been diluted due to the heterogeneity of the externalizing group and comorbidity across domains. Although a distinction was made between externalizing and comorbid youths, demarcation between groups may be artificial and could be due to poor detection of internalizing symptoms in externalizers at the time of clinical interview. Findings from

Scott and colleagues [42] study reporting high levels of psychological distress and mental health problems in headspace clients, gives weight to the heterogeneity of the headspace population and supports views that young people with multiple disorders are more likely to seek help than young people with single disorders [91]. Our findings do raise questions with regard to disorder characterization and challenges the categorical nature of diagnoses. A more useful theoretical model for conceptualizing child and adolescent neuropsychiatric disorders may be to use a dimensional approach that incorporates duration of disorders and number of risk factors involved.

Other interesting findings from the second study relate to the male to female ratio found in the comorbid group, with equal numbers of both gender. Including females in the comorbid group led to an overall improvement in EF. When females were removed, the remaining males exhibited poorer EF. This suggests further research exploring gender differences in neuropsychological impairment for young people with psychopathology may be useful. Females with externalizing disorders may also experience high levels of internalizing disorders when compared with externalizing males. The results from the first study would suggest this, as both the predominantly male, early and late onset youth, showed mild levels of depression and anxiety. However, when participants from the first study were included in a larger externalizing group in the second study, the predominantly male group, showed moderate to severe levels of anxiety and depression. It is unclear how the externalizing group in the second study differed from the more specific CD groups in the first study on severity of comorbid anxiety and depression. As the externalizing group comprised of participants with mixed ADHD, ODD and CD, some of these disorders may predispose to internalizing disorders more than others.

These findings support a dimensional approach to understanding childhood psychopathology, encompassing gender differences in the development of disorders. High comorbidity across and between domains was demonstrated in these results and therefore suggests that youth experiencing multiple mental health problems exhibit worse outcomes in cognitive function. Further research into neuropsychological profiles of early onset psychiatric disorders in youth, can provide opportunities for early detection of accompanying cognitive impairments and hence, more targeted treatment options. For example, awareness of verbal learning and memory deficits in early onset CD, suggests that treatment encompassing the strengthening of these deficits may assist in the improvement of overall functioning. As high comorbidity was found between the externalizing and internalizing domains, assessing externalizing youth for comorbid internalizing disorders is essential for treatment delivery. Further investigation into gender differences in the development of psychopathology may also be warranted.

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Statement of Contributions

Declaration by candidate

Chapter 1 has been submitted for publication. The title and co-authors are as follows:

Johnson VA, Kemp, AH, Heard, R, Lennings, CJ, Hickie, IB. Childhood versus Adolescent Onset Antisocial Youth with Conduct Disorder: Focus on Psychiatric Illness, Neuropsychological and Psychosocial Function

The nature of my contribution to the work included the following:

- Project conception
- Experimental design
- Statistical design
- Data collection
- Data analysis

- Data interpretation
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The following co-authors contributed to the work. The nature of their contribution is listed below.

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Chapter 2 has been submitted for publication. The title and co-authors are as follows:

Johnson, VA, Kemp, AH, Lennings, CL, Guastella, AJ, Heard, R, , Hermens, D., Hickie, IB. Externalizing versus Internalizing Disorders in Young People: Focus on Neuropsychological and Psychosocial Function.

The nature of my contribution to the work included the following:

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The undersigned hereby certify that:

1. The above declaration correctly reflects the nature of the candidate's contribution to this work and the nature of the contribution of each of the co- authors.
2. They meet criteria for authorship in that they have participated in the conception, execution or interpretation of the work relevant to their field of expertise.
3. They take public responsibility for their part in the publication, except for the senior author who accepts overall responsibility for the publication.
4. There are no other authors of the publication.
5. Potential conflicts of interest and declarations of financial support have been disclosed to the editor and/or publisher of the academic journal.

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