British Journal of Learning Disabilities
The Official Journal of the British Institute of Learning Disabilities

Adults with Intellectual Disability and ADHD: Clinical characteristics and medication profiles

Journal:	*British Journal of Learning Disabilities*
Manuscript ID	BLD-18-0047.R2
Manuscript Type:	Original Article
Keywords:	ADHD, Autism, Challenging behaviour

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Abstract

The diagnosis of ADHD is often missed or misdiagnosed in people with Intellectual disability (ID). Despite a significant growth in literature on the diagnosis and treatment of ADHD in people without ID, there have been few studies on ADHD in people with ID. In this paper, we describe a group of adults with ID and ADHD open to a specialist community ID service. We examined the frequency and dose of antipsychotic use and considered whether ADHD medication is associated with a reduced use of psychotropic medication. The study found a high incidence of autism in people with ID and ADHD. Men with ID were given the diagnosis of ADHD more often compared to women with ID. Only 36% of people with ADHD and ID taking ADHD medication were on antipsychotic medications compared to 93% of people with ADHD and ID without ADHD medications. This generates several hypothesis such as whether antipsychotic medications are prescribed to control ADHD symptoms, whether use of ADHD medications can reduce the use of antipsychotic medications and/or whether antipsychotics are used to treat underlying psychiatric comorbidities in people with ADHD. Randomised controlled trials are needed to answer the question whether use of ADHD medication reduces use of antipsychotic medication in people with ID and ADHD. Further studies are also needed to explore reason for not using ADHD medication in certain patients with ADHD and ID and what treatment options are effective in treating psychiatric comorbidities in people with ADHD and ID.

Accessible summary:

- ADHD is often missed/underdiagnosed in people with ID compared to people without ID
- Presence of ID, autism and challenging behaviour should raise the suspicion of ADHD as comorbid neurodevelopmental disorder
- Treatment of ADHD in people with ID may reduce the need for antipsychotic medications

Introduction

ADHD in Intellectual Disability

Intellectual Disability (ID) is defined as a neurodevelopmental disorder with onset during the developmental period with deficits in both intellectual and adaptive functioning in conceptual, social, and practical domains. An overall prevalence of ID in the general population was shown to be approximately 1.04% (Maulik, Mascarenhas, Mathers, Dua, & Saxena, 2011). The presence of one neurodevelopmental disorder (NDD) is known to increase the co-occurrence of other neurodevelopmental disorders (NDD). Therefore, it is important to consider other NDDs in people with intellectual disability.

DSM V defines ADHD as a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development (American Psychiatric Association, 2013). The diagnosis of ADHD in adults requires five or more symptoms to be present in hyperactivity/impulsivity and/or inattention domains and before the age of 12 years. The symptoms must be evident in two or more settings and associated with functional impairment. Although ADHD is commonly associated with children, studies have shown that

it persists during adolescence and adulthood in up to two-thirds of individuals and as full or partial persistence causing a functional impairment (Barkley, Fischer, Smallish, & Fletcher, 2002; Lara et al., 2009).

ADHD affects an estimated 3.4% of the adult population with worldwide estimates of 1.2-7.3% (Fayyad et al., 2007, 2017). It is more prevalent in people with ID compared to the non-ID population causing a significant functional impairment (Able, Johnston, Adler, & Swindle, 2007). Several studies have shown a higher prevalence of ADHD in adults with ID ranging from 8.7% - 20.4% (Cantwell, 1996). A Swedish cohort study showed that "people with ID were at increased risk of ADHD compared to those without ID, and relatives of people with ID were at increased risk of ADHD compared with relatives of those without ID" (Faraone, Ghirardi, Kuja-Halkola, Lichtenstein, & Larsson, 2017). Shared genetic risk factors and a strong familial association may explain the comorbidity between ADHD and ID (Voigt, Barbaresi, Colligan, Weaver, & Katusic, 2006). Studies comparing people with ID to people without ID have shown that people with ID continue to have more symptoms of ADHD compared to people without ID from childhood to adulthood (Xenitidis, Paliokosta, Rose, Maltezos, & Bramham, 2010). Therefore, the evidence for assessing adults with ID for ADHD is compelling. Furthermore, it can be argued that diagnosing of ADHD in people with ID is even more important given it is the only diagnosis among NDDs such as Autism, ID, dyslexia and dyspraxia which has an evidence-base of effective pharmacological treatments. For example, a review concluded that psychostimulants (such as methylphenidate, dexamphetamine, mixed amphetamine salts and lisdexamfetamine) and non-psychostimulants (such as atomoxetine) are significantly more efficacious than placebo for

treating ADHD (De Crescenzo, Cortese, Adamo, & Janiri, 2017). Authors also suggested that there was only preliminary evidence for the effectiveness of non-pharmacological treatments of ADHD in adults.

Under diagnosis of ADHD in ID

As highlighted by the World Health Organisation, people with learning disabilities experience various health inequalities; they have more chronic conditions than the general population, they develop chronic health conditions at a younger age, and also die sooner following diagnosis (World Health Organization [and] The World Bank, 2011). Moreover, it has been reported that there is an increase of ADHD symptoms in ID, which "could not be explained by inappropriate expectations or by confounding associations with other emotional/behavioural or cognitive problems" (Simonoff, Pickles, Wood, Gringras, & Chadwick, 2007) Despite this, ADHD is often considered as under-recognised in people with intellectual disability (Rose, Bramham, Young, Paliokostas, & Xenitidis, 2009) and recognising it can be challenging for multiple reasons (Perera & Courtenay, 2017). The core signs of ADHD of inattention and hyperactivity can also be manifestations of ID (Deb, Dhaliwal, & Roy, 2008). There is also the added factor of a higher prevalence rate of Autism in ID, which may make the diagnosis of ADHD even more complex. Problems associated with ADHD and their presentation are reported to vary depending on age (Montano, 2004; Rutter et al., 2011) where hyperactivity may present as extreme activity in a younger child compared to restlessness in an adult. Given that adults with ID have lower intellectual functioning compared to their chronological age, use of symptoms in adults without ID for diagnosing ADHD in ID population may not be accurate. The DSM V criteria for ADHD

include several symptoms, which can only be detected in people with verbal communication skills. A majority of people with severe ID have significant deficits in their expressive and comprehensive communication skills and therefore these criteria may not be applicable (Perera, 2018). Having a pyschiatric co-morbidity can make the diagnosis of ADHD difficult ; two thirds of people with ADHD have at least one psychiatric comorbidity with an average number of co-morbidities of 2.4 per person (Piñeiro-Dieguez, Balanzá-Martínez, García-García, Soler-López, & CAT Study Group, 2016). A high prevalence of mental illness in people with ID (Cooper, Smiley, Morrison, Williamson, & Allan, 2007) with a co-existent diagnosis ADHD can complicate the initial diagnosis and subsequent management of these underlying mental health issues.

A recent review reported that antipsychotic medications are used in people with ID and challenging behaviour in the absence of a severe mental illness (Sheehan et al., 2015). In the ID/ADHD population we hypothesise that antipsychotics are used to manage ADHD symptoms, where ADHD medication should be the preferred treatment choice.

Study aim

The study is part of a service evaluation project of people with ID and ADHD as a response to NHS England's 'stopping over medication of people with learning disability, autism or both with psychotropic medications' (STOMP) campaign to stop the overuse of medications (NHS, 2018). We aimed to evaluate people with ID and a diagnosis of ADHD and treatment pathways in a specialist community ID service. We describe characteristics of the group of

adults with ID and ADHD; the frequency and dose of antipsychotic; and whether ADHD medication is associated with reduced psychotropic use.

Methods

Study design and sample requirement

A psychiatry case register of people with intellectual disability and mental health difficulties open to the service were accessed for the period of 1 August 2017 to 1 September 2017. Inclusion criteria were as follows : 1) Formal diagnosis of intellectual disability 2) age greater than 18 years 3) Confirmed diagnosis of ADHD. The validity of the diagnoses of ADHD and ID was confirmed by inspecting the clinical records. Furthermore the diagnosis of ADHD was confirmed by a consultant psychiatrist in intellectual disabilities using clinical impression and DSM V criteria. Exclusion criteria included : 1) patients under the age of 18 years 2) unclear diagnosis of ADHD (insufficient records to make diagnosis/not formally diagnosed by a mental health professional/not present in adulthood/ insufficient evidence when correlated with clinical impression and DSM V) 3) borderline intellectual disability 4) Individuals no longer active on the case register at time of study (travel abroad/non compliance with service).

Setting

The location of the study was in the London Borough of Haringey where over two thirds of the community are from ethnic minorities and over 100 languages are spoken. In the borough there are areas of great social deprivation. These socio demographic factors can add to the complexity of mental health diagnosis and treatment, however the diversity of this

study sample makes the findings more applicable to different patient groups given it represents a group of people with multiple genetic variability to social diversity. The case series was conducted in Haringey Intellectual Disability services in London, a specialist integrated Intellectual Disability service providing health and social care inputs to adults with Intellectual disability living in the borough.

Data collection

Data was extracted from the records to include demographic data: age, gender, and severity of ID (mild, moderate, severe). Severity of ID was determined using intelligence quotient (IQ) in parallel with the level of adaptive and social functioning for that individual. Information on comorbid mental health problems (categorised in accordance with DSM V criteria) and current psychiatric medications (divided into antipsychotics, anxiolytics and hypnotics) were collected along with the use of stimulant and non-stimulant ADHD medication.

The frequency and dosage of antipsychotic use in this group was also assessed. Dosage was given as a percentage of the maximum recommended dose for the antipsychotic in the British National Formulary (BNF) (Joint Formulary Committee, 2017). This is a reliable tool for standardizing antipsychotic doses in drug utilization research (Nosè et al., 2008; Sweileh et al., 2014). When two antipsychotics were used the individual percentages of the maximum dose were added to give a total percentage. Patients receiving a percentage of BNF maximum >100% were considered to have a high dose. The medications given and dosages prescribed vary throughout each individuals treatment pathway. The results described represent the medication profile at the time of data extraction (1 September 2017).

Data analysis

Data were analysed using SPSS version 20.5. All variables were tested for normality using visual inspection and Shapiro-Wilk test. Differences between the groups were assessed with independent sample t-test. Pearson product-moment correlation coefficient was used to calculate correlation. An independent-sample t-test was conducted to compare antipsychotic dose in patients who were using ADHD medication compared to those who were not. The Shapiro-Wilk test with a Q-Q plot was used to assess for normality. A Pearson product-moment correlation coefficient was also computed to assess the relationship between antipsychotic dose as a percentage of maximum BNF recommended dose compared to ADHD medication dose as a percentage of the maximum BNF recommended dose.

Results

A total of 32 people with ID and ADHD were identified during the study period. Three were excluded as there was an unclear diagnosis as a result of insufficient information on ADHD status in adulthood. Data extraction and analysis were conducted on the remaining 29 cases who met inclusion criteria. Descriptive statistics are presented in Table 1.

The diagnosis of ADHD was 6 times more prevalent in men than women in this group. More than half (55%) had severe intellectual disability. Downs syndrome was present in two cases and Smith Magenis syndrome in one.

Table 1: Case series characteristics (n = 29)

Mean Age (Years)	Gender	Severity ID	Co-morbid Diagnoses	Psychotropic use
26.3	Male 25 (86%)	Mild 5 (17%)	Autism 22 (76%)	Antipsychotic 23 (79%)
	Female 4 (14%)	Moderate 8 (28%)	Anxiety Disorder 6 (21%)	Anxiolytics 14 (48%)
		Severe 16 (55%)	Mood Disorder 5 (17%)	Hypnotics 6 (21%)
			Genetic Disorder 3 (10%)	
			Psychotic Disorder 1 (3%)	
			Tic Disorder 2 (7%)	
			Personality Disorder 1 (3%)	

Co-morbid diagnoses and psychotropic medication

In this series 22 (76%) met the diagnostic criteria of autism spectrum disorder. Anxiety and mood disorders were the other two most common diagnoses with a prevalence of 21% and 17% respectively. The prevalence of psychotic disorders and personality disorders was 3%. Comorbid psychiatric disorders did not correlate with using psychotropic medication. 79% of people with ADHD were using antipsychotic medication and 48% anti-anxiety medication. Fourteen people (48%) were using ADHD medication and of these 12 (86%) were using Atomoxetine and 2 (14%) Methylphenidate slow release preparations.

Antipsychotic use and ADHD

The antipsychotic profiles are summarised in tables 2 and 3. Twenty (69%) were using one antipsychotic drug and 3 (10%) were using two antipsychotics. Six (21%) were not using antipsychotic medication. None exceeded the maximum BNF recommended dose with majority (62%) on less than 25% of the recommended maximum dose. Fourteen were using ADHD medication, of which 5 (36%) were not using concomitant antipsychotic. Fifteen people with a diagnosis of ADHD were not using ADHD specific medication but were using antipsychotic medication of whom 3 (20%) were using two antipsychotics. There was no significant difference in antipsychotic dose in those using ADHD medication (M=27, SD=34) and those not (M=28, SD=23); t (27) = 0.145, p=0.886. There was no correlation between antipsychotic and ADHD medication dose, r- 0.201, n=29, p=0.295.

Table 2: Antipsychotic profile in all patients with ADHD (n = 29)

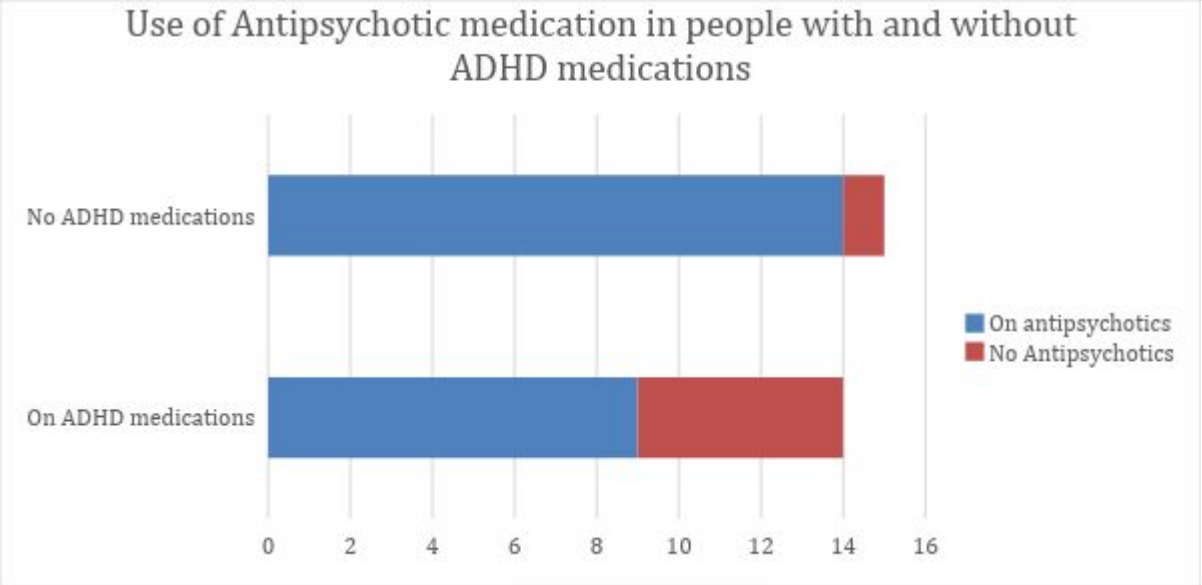
Number of antipsychotics	Frequency (n=29)

0	6 (21%)
1	20 (69%)
2	3 (10%)
Percentage of maximum BNF recommended dose	
0-25%	18 (62%)
25-50%	6 (21%)
50-75%	3 (10%)
75-100%	2 (7%)
>100%	0 (0%)

Table 3: Antipsychotic profile of patients taking and not taking ADHD medication.

	On ADHD Medication (n=14)	Not on ADHD Medication (n=15)
Number of antipsychotics		
0	5	1
1	9	11
2	0	3
Percentage of maximum BNF recommended dose		
0-25%	9	9
25-50%	1	5
50-75%	3	0
75-100%	1	1

Mean % of maximum dose	27	28
Standard deviation of % of maximum dose	34	23



Discussion

The service evaluation has raised important questions with regard to the diagnosis and treatment of ADHD in a group of people with ID and challenging behaviour. We argue that there is not enough emphasis on ADHD as a neurodevelopmental disorder (NDD) in people with ID. Presence of one NDD is known to increase the risk of another NDD. Therefore, given ID as a NDDs, ADHD should be looked into in patients with ID. This is further supported by NICE (2018) Guidelines on ADHD recognising people with ID as a high risk group (NICE, 2018). Autism Spectrum Disorder in ID population is more often recognised and accepted compared to ADHD. Studies have shown that prevalence of ASD in people with ID is to be around 30 - 65% (Clark, Feehan, Tinline, & Vostanis, 1999; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008). The prevalence of autism in adults with ADHD and ID has not been reported in current literature. However in our series, the prevalence of autism in adults with ID and ADHD was 76%. The high prevalence reported may be a reflection of the increased risk of NDDs seen when one NDD is already present.

ADHD is diagnosed and treated more often in males than in females with a ratio of approximately 3:1 (Cantwell, 1996). According to Arnett *et al* (2015), males showed more severe symptoms and significantly more variance compared to females (Arnett, Pennington, Willcutt, DeFries, & Olson, 2015) . We observed a higher male: female ratio of 6:1 in people with ID. A similar argument that men with ID show more severe symptoms and more variance which makes it easy to detect ADHD symptoms in men with ID may explain the reasons behind the high male to female ratio in ID in this study.

Diagnosis of ADHD can be considered challenging with increasing severity of ID. However, the majority (83%) in our case series had moderate to severe intellectual disability. This is in keeping with the current literature where the risk of ADHD increases with the severity of ID (Voigt et al., 2006). This shows that the diagnosis of ADHD can be considered irrespective of the severity of ID. Even though the study did not look into subtypes of ADHD , it is likely to that the diagnosis was made by the behaviour of the individual which meets the criteria for hyperactivity/impulsivity domain of DSM V criteria.

This study raises various clinical conundrums and hypotheses. Challenging behaviour is common in people with ID. It is defined as “behaviour of an intensity, frequency, or duration that threatens the physical safety of the person or others or restricts access to community facilities” (Emerson, 2001). Symptoms of inattention, distractibility, impulsivity, and hyperactivity in ADHD can be perceived as challenging behaviour in people with ID. Studies have also shown that children with ID and ADHD are likely to have more conduct problems compared to children with ADHD without ID (Ahuja, Martin, Langley, & Thapar, 2013). Authors also reported that the presence of ADHD and ID combination increases the risk of Oppositional Defiant Disorders and Conduct Disorders compared to children with only ID or only ADHD. This shows the importance and complexities in diagnosing ADHD in people with ID along with the high rate of suspicion needed in children with ID for behavioural disorders. These may result in ADHD being missed in people with ID and challenging behaviour leading to inappropriate treatments such as use of antipsychotic medications. This may be one of the explanations for the recent findings that 71% of patients with ID were using psychotropic drugs without a recorded severe mental illness in order to manage their ‘mood

dysregulation' (Sheehan et al., 2015). These findings were also replicated in a study looking at prescribing in people with autism (Cvejic, Arnold, Foley, & Trollor, 2018). This is also paralleled by our series where 79% were using antipsychotic medication despite only 3% having a psychotic disorder. This raises the question why antipsychotic medications are used in this patient group off label. A case series of 61793 children reported that about 1 in 5 children with a diagnosis of ADHD and long acting stimulant medications were also on a second generation antipsychotic (Kamble, Chen, Johnson, Bhatara, & Aparasu, 2015). Studies have also shown that the presence multiple psychiatric comorbidities as a single most predictor of polypharmacy and off label prescribing (Kearns & Hawley, 2014). This suggests that antipsychotic medications may be used for different purposes in patients with ID, ADHD and challenging behaviour. One hypothesis is that antipsychotic medications may be used to treat underlying comorbid psychiatric disorders such as anxiety disorders.

There are several downfalls associated with the use of psychotropic drugs in people with ID without a severe mental illness. Although psychotropic drugs can reduce anxiety and improve sleeping patterns, there is no strong evidence base to support use of antipsychotic medications to treat the core symptoms of ADHD. Long-term antipsychotic use also has several side effects such as metabolic syndrome, weight gain, hyperprolactinaemia and sedation (McQuire, Hassiotis, Harrison, & Pilling, 2015). This study showed a clear difference in the use of antipsychotic medications between the two groups of people with ID and ADHD who take ADHD medication versus those not on ADHD medications. People who are not using ADHD medications were more likely to use one or more antipsychotics while those using ADHD medication used fewer antipsychotic medication. This raises the question whether ADHD medication use can reduce the use of antipsychotics. This association needs

to be explored through more robust research methodologies. However, this small case series suggests that the use of ADHD medications may be beneficial to reduce use of antipsychotics in people with ID.

Stimulant (Methylphenidate) and non-stimulant (Atomoxetine) medication are the main pharmacological treatment options for ADHD both in the non-ID (Contini et al., 2013) and ID population (Ji & Findling, 2016). However, less than 50% in our series were using any form of ADHD medication. The reasons for this may include withdrawal as they progress into adulthood, lack of efficacy, intolerable side effects, family refusal, and/or clinician oversight. When comparing people who were using ADHD medication with those without there was no statistical difference in antipsychotic dose and no correlation between ADHD dose and antipsychotic dose. However, it is difficult to ascertain whether several confounders such as severity of ADHD, severity of ID, prescribing clinician, and co-morbid disorders that were not addressed could have an impact on psychotropic dosing.

The effective diagnosis and treatment of ADHD can result in considerably reducing psychosocial burden. This is of particular importance, as there is a high functional and psychosocial impairment associated with adult ADHD including parental history of anxiety, dissatisfaction with love life, and consumption of tobacco (Moulin et al., 2018). Untreated ADHD could also contribute to functional impairment and occupational outcomes; for example, a cross-sectional study has demonstrated that “later age of first central stimulant treatment for ADHD and higher inattentiveness ratings were associated with lower level of employment” (Gjervan, Torgersen, Nordahl, & Rasmussen, 2012). Prompt treatment can

also affect long term outcomes, such as academic, antisocial behaviour, driving, non-medicinal drug use/addictive behaviour, obesity, occupation, services use, self-esteem, and social function outcomes; it has been shown that ADHD treatment improved long-term outcomes compared with non-treatment, even though the outcomes did not reach normal levels (Shaw et al., 2012).

The combination of a high prevalence of ADHD and diagnostic overshadowing in the ID population warrants the development and routine use of a screening tool for ADHD tailored specifically towards the ID population. We also suggest that the high rate of co-morbid autism in ADHD/ID should prompt every clinician in considering autism spectrum disorder as an additional diagnosis.

Limitations

There are several limitations in our study. As this is a local series with a sample size of 29 these findings cannot be generalised to the ID/ADHD population as a whole. The series used a retrospective medical record review and therefore there may have been incomplete or missing data as well as difficulty in interpreting or verifying the documented information.

Future Research

Although ASD and ADHD are distinct disorders according to DSM-5, there is still a considerable genetic and clinical overlap between them (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010; Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011). Mayes *et al* (2011) reported that children with ADHD did not present with many of the

symptoms on the Autism Screening Checklist and therefore children with autism can distinguished from children with ADHD (Mayes et al., 2011). However, children with Autism showed some of the symptoms such as inattention, impulsivity, and hyperactivity in maternal rating scales. Challenges in differentiating the two disorders in clinical practice may result in people with ADHD either under or over diagnosed in people with Autism. Further studies are needed to explore symptomatology which can be used to differentiate ADHD from Autism.

Summary

ADHD is a neurodevelopmental disorder which is often neglected in people with ID. There are diagnostic challenges related to ADHD in ID, however it is an important diagnosis to be considered given the strong evidence base and national guidelines when diagnosing and treating ADHD. Autism and ADHD appear to have highly comorbid in people with ID. This case series showed that only a smaller number of patients who take ADHD medications were on Antipsychotic medications compared to patients who were not taking ADHD medications. This raises clinical questions whether ADHD is treated using antipsychotics rather than evidence based pharmacological treatments as per national guidelines. More research is needed in people with ID and ADHD.

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