Co-Morbid Depression in Autism Spectrum Disorder – A Closer Look at the Diagnostic Challenges

Abstract

Despite widespread evidence for it' elevated prevalence, depression remains an understudied comorbidity in Autism Spectrum Disorder (ASD). This review examines the difficulties associated with diagnosing depression across the spectrum, emphasising the significance of the vast diversity of ASD presentation. It investigates the sensitivity of current diagnostic methods, considering reported differences in prevalence as a function of shortcomings of current diagnostic tools as opposed to actual differences in susceptibility to depression. Taken together, the vast phenotypic heterogeneity of ASD teamed with indications of atypical symptomology suggest that current diagnostic tools may be of limited value for use with the ASD population.

Major Depressive Disorder

Major depressive disorder (MDD) represents one of the most common psychiatric conditions observed in the clinical setting today (Fasick et al., 2015). While prevalence rates vary significantly according to gender (Hankin et al., 2015), age (Hoertel et al., 2015) and culture (Ferrari et al., 2013a), recent estimates suggest that MDD affects 350 million people globally (World Health Organisation, 2016). Its chronic and often recurrent nature (Mars et al., 2015) teamed with its significant impact on functionality (Greenberg et al., 2015), make depression the second leading cause of disability worldwide (Ferrari et al., 2013b).

While major life stressors are widely understood to constitute the strongest risk factor for MDD (Slavich and Irwin, 2014), in practice the aetiology of depression is complex and multifaceted, encompassing a number of biochemical (Osso et al., 2016), genetic (Dunn et al., 2015), inflammatory (Valkanova, Ebmeier, Allan, 2013), social (Rueger et al., 2016) and psychological (Cheng et al., 2015) components. However, despite vast scientific advances, both the individual and interactive effects of each of these aetiological factors remain contentious and unclear (Dowrick, 2016). As such, there are still no widely accepted diagnostic biomarkers of the disease (Phillips et al., 2015). Given these controversies, it has been postulated that MDD may in fact represent several syndromes that differ in aetiological origin and symptomatic presentation as opposed to a single unified disease entity (Fried and Nesse, 2015b). Treatment of MDD also remains a provocative and actively investigated area of research, with the efficacy of both psychological interventions (Driessen et al., 2015) and anti-depressant medication (Kirsch et al., 2008) still fiercely disputed.

MDD is currently identified using a combination of clinical interview and standardised screening instruments (Nezu et al., 2014). In order to meet DSM-5 diagnostic criteria for MDD, an individual must experience continuous depressed mood or anhedonia for two weeks or more, in addition to four of the following: weight change, loss of energy, altered sleep patterns, difficulty concentrating, feelings of worthlessness or guilt, psychomotor change, and suicidal ideation (APA, 2013). Importantly, DSM-5 updates added that clinical judgement is required to disentangle depression from a normal bereavement response. While this inclusion of subjectivity may impair the clinical reliability of MDD (Tandon, 2015), this move has generally been welcomed as an acknowledgment that fixed diagnostic criteria may struggle to encapsulate the myriad of possible symptomatic expressions of the disorder (Sexton, 2015).

Diagnosis of MDD is complicated by frequent co-morbidity (Deschênes, Burns and Schmitz, 2015) and significant symptomatic overlap (Goldberg, 2016) with a host of other mental and physical conditions. However, understanding of the disorder is particularly hampered by a lack of consensus of what actually constitutes a depressive state. There is disagreement regarding the diagnostic boundary between ordinary sadness and major depression, with Wakefield and Schmitz (2013) reasoning that there is no empirically defined basis for the current cut-off of five symptoms for two weeks. Accordingly, Goldberg (2011) argues that the diagnosis of MDD based solely on the presence or absence of these depressive symptoms is over-simplistic and reductionist. In practice, the literature indicates that depressive states represent a continuum (Maj, 2016).

Current conceptions of the symptom profile of MDD have evolved and expanded as our knowledge of the disorder has grown (Monroe and Anderson, 2015). Despite this, the case has been made that today’s diagnostic criteria still do not recognise the full scope of symptoms that MDD may encompass (Fried and Nesse, 2015a). In fact, Patten (2015) argues that it may be impossible to condense the disorder’s complexity down to any concise list of diagnostic criteria. This lack of consensus, teamed with evidence that clinical sub-groups may present with depressive symptoms distinct to those in the general population (Scott and Havercamp, 2015), makes the co-morbid diagnosis of MDD in a disorder such as ASD particularly challenging.

Autism Spectrum Disorder

Come a long way from its original description as a “disturbance of affective contact” (Kanner, 1943), Autism Spectrum Disorder (ASD) is today conceptualised as a lifelong neuro-developmental disorder characterised by two central dimensions; social-communication impairments and restrictive, repetitive behaviour patterns (APA, 2013). While these subdomains are thought to broadly capture its core features (Lai et al., 2013), ASD demonstrates phenotypic heterogeneity so extensive that it is now widely established as a defining feature of the disorder (Hervas, 2016; Kim et al., 2016). Individuals with ASD exhibit a vast continuum of social (Rice et al., 2012), communicative (DiRezze et al., 2016) and behavioural (Bishop et al., 2013) deficits, varying significantly in the level of impairment shown in each domain, and in turn the level of care required (McPartland, Law and Dawson, 2015).

While classically described symptoms include difficulty understanding non-verbal cues and intense preoccupation with routine (APA, 2013), in practice ASD encompasses a hugely diverse spectrum of symptoms. There are vast differences in symptom severity (Bora et al., 2016), with associated impairment existing on a continuum varying from sub-clinical to severe (Wijngaarden-Cremers et al., 2014). Functionally, individuals range from fully verbal to non-verbal (Georgiades, Szatmari and Boyle, 2013) and above-average to low IQ (Charman et al., 2011). Phenotypic heterogeneity of this scale creates an obvious clinical challenge.

Despite wide consensus for a strong genetic basis (Huguet, Benabou and Bourgeron, 2016), like MDD, the aetiology of ASD is multi-faceted and complex (Shaw, Sheth and Tomlhenovic, 2014). Complicating matters further, Happé and Ronald (2008) postulate that the classically described triad of symptoms (Rutter, 1968) are in fact ‘fractionable’ – each defined by independent genetic origins (Robinson et al., 2012) – a hypothesis for which supportive evidence is growing (Brunsdon and Happé, 2014). However, with the central molecular pathways currently elusive (Happé, 2011) and largely unclassified (Chen et al., 2015), both diagnosis (Constantino and Charman, 2016) and treatment (Goldstein and DeVries, 2013) of ASD focus exclusively on behavioural features. With recent prevalence estimates of 1.5% (Centers for Disease Control and Prevention, 2014), ASD represents a substantial public health concern (Park et al., 2016).

Introduction of the DSM-5 brought substantial modifications to the diagnostic paradigm underpinning ASD. Previously described as a triad of impairment (APA, 1994), the three original dimensions were condensed into two; with restrictive/repetitive behaviour patterns remaining unchanged but social and communication deficits being merged into one subdomain (APA, 2013). While welcomed by some as an improvement in clarity (Lai et al., 2013), this revision was also met with criticism, with Wing et al. (2011) arguing that assessment of social and communicative impairments as distinct entities provides utility in a clinical context.

Perhaps most significantly, DSM-5 also moved from a categorical classification model to a dimensional one (Ousley and Cermark, 2014); no longer recognising the existence of formerly discrete entities such as Asperger’s syndrome or Autistic Disorder. Instead, all four previous diagnoses are subsumed by the single over-arching diagnosis of Autism Spectrum Disorder, supplemented with severity scales for each of the two central dimensions. While a growing body of research has identified discrepancies in the proportion of people qualifying for diagnosis under DSM-5 criteria compared to DSM-IV-TR (Bennett and Goodall, 2016), research regarding the validity and reliability of ASD as a new diagnostic category is mixed and on-going (Smith, Reichow and Volkmar, 2015).

As such, far from denoting a static neurodevelopmental disorder category, ASD represents a complex, fast-changing diagnostic concept (Volkmar and McPartland, 2014), of which current knowledge is sparse and highly fragile (Georgiades, Szatmari and Boyle, 2013). While the past two decades have seen significant advancement (Verbelchuk and Kwon, 2013), the classification, aetiology and management of ASD remain shrouded in contradiction and uncertainty (Goldstein and DeVries, 2013). Ambiguity of this nature impedes understanding of co-morbid psychiatric conditions.

Depression in ASD – An Introduction

It is well-established that individuals with ASD are significantly more likely to experience depressive symptoms compared to the general population (e.g. Croen et al., 2015; De-la-Iglesia and Olivar, 2015; Strang et al., 2012). Despite this, depression remains an understudied and overlooked comorbidity within the ASD literature (Greenlee et al., 2016). Ascertaining accurate estimations of prevalence rates has proven extremely difficult – with figures ranging from 7% (Greenlee et al., 2016) to 70% (Lugnegard et al., 2011). Clear methodological limitations within the literature such as small sample sizes, use of different assessment instruments and a lack of diagnostic tools specifically validated for use with the ASD population (Sterling et al., 2015) go far in explaining these disparities.

While mechanisms underlying the co-morbidity currently remain unclear, a number of explanations have been postulated. For example, it has been argued that cognitive rigidity (Gotham et al. 2014) combined with difficulties comprehending the temporal durability of present states (Storch et al., 2013) may incline an individual with ASD towards inflexible, depressogenic rumination. The observation that poor emotion regulation commonly presents in ASD has also been stipulated as contributory (Bruggink et al., 2016), given that maladaptive coping strategies predict depression in both ASD (Santomauro, Sheffield and Sofronoff, (2016) and neurotypical populations (Pouw et al., 2013). Individuals with ASD are additionally exposed to a range of risk factors for secondary depression including social isolation (Cassidy et al., 2014), bullying (Pouw et al., 2013), unemployment (Roux et al., 2013) and anxiety (Kerns et al., 2015). Family history of depression has also been identified as predictive (Gadow, Devincent and Schneide, 2008).

There are a number of important motives for improving the diagnosis of co-morbid depression in ASD. Depressive symptoms elicit poorer global functioning (Mazzone et al., 2013), impede therapeutic progress (Ameis and Szatmari, 2015) and increase burden on caregivers (Chandrasekhar and Sikich, (2015). Furthermore, depression can exacerbate the central features of ASD itself (Greenlee et al., 2016), reducing functionality and subsequent quality of life (Kuhlthau et al., 2010). This, teamed with the recent accumulation of evidence demonstrating increased suicide risk in ASD (Segers and Rawana, 2014) indicates the pressing need for better identification of depression in the ASD population.

This review seeks to address two main questions: 1) What are the specific practical and theoretical challenges associated with diagnosing depression in Autism Spectrum Disorder? 2) To what extent may reported disparities in depression prevalence be an artefact of poor diagnostic sensitivity across the full spectrum of ASD presentation?

Diagnosing Depression in ASD – Practical Difficulties

As it stands, an individual with ASD presenting with depressive symptoms is diagnosed using a combination of conventional methods including self-report and semi-structured interview (Ozsivadjian, Hibberd, and Hollocks, 2014). However, utilisation of diagnostic instruments designed for use with the general population rather than individuals with ASD (Mazzone et al., 2013) poses a number of significant problems.

Clinical assessment of the majority of DSM-5’s MDD criteria capitalises on an individual’s ability to articulate their moods, feelings and emotions. Communicative difficulties and impairments in social-emotional reciprocity (APA, 2013) create unique challenges for this feat – often rendering the expression of internal states such as low mood, anhedonia and low self-esteem profoundly difficult (Richa et al., 2014). However, conveying depressive symptomology to a practitioner relies not just on communicative abilities, but also on the capacity for self-awareness, which is often compromised in ASD (Schriber, Robins and Solomon, 2014). Awareness of depressive thoughts and feelings in the self requires introspective capabilities and insight (Gotham, Unruh and Lord, 2014), both of which appear to be reduced in autism spectrum disorder (Ousley and Cermark, 2014). If Individuals with ASD lack the ability to introspect (Schriber, Robins and Solomon, 2014) and label (Samson, Huber and Gross, 2012) their internal thoughts and emotions, it follows that they may be less self-aware of depressogenic thoughts and feelings in the first place.

Originally described in a seminal study by Baron-Cohen, Leslie and Frith in 1985, theory of mind deficits are widely established as a common feature of ASD (Sodian, Schuwek and Kristen, 2015). Defined as impaired understanding of the thoughts, emotions and intentions of the self and others (Washburn et al., 2016), individuals classically struggle to comprehend the internal states of those around them. These deficits have important implications for the diagnosis of depression in this unique sub-population. Impairments in theory of mind can disguise psychiatric disorders (Mazzone et al., 2013), with Lombardo and Baron-Cohen (2011) arguing that the neurocognitive underpinnings of poor attribution of internal states apply strongly to understanding of these feelings in the self.

Importantly, self-awareness is a complex and vastly multi-dimensional construct (Zahavi, 2010), making global or universal deficits unlikely. For example, populations with ASD show significant insight into their own personality (Schriber, Robins and Solomon, 2014) and memory performance in a recall task (Elmose and Happé, 2014). However, disordered processing and understanding of emotion in the self is well-documented in the ASD literature (Silani et al., 2008; Bird and Cook, 2013). As such, rather than a global deficit, it is more likely that ASD involves selective impairments in self-awareness (Williams, 2010). If people with ASD are less able to identify their own moods and emotions, it follows that self-report and interview techniques may not represent fruitful means of identifying depressive symptomology in this clinical sub-group.

Accordingly, a growing body of research has documented alexithymia (defined as difficulty identifying, labelling and describing emotions in the self - Cook et al., 2013) in ASD (Milosavljevic et al., 2016). In fact, Chandrasekhar and Sikich (2015) found that depressed individuals with ASD rarely directly articulate subjective states of sadness or suicidal ideation. Accordingly, ASD populations do not report the full scope of their depressive symptoms (Storch et al., 2012), with Lambert et al. (2016) observing young people with ASD to describe an absence of sleep problems despite clear evidence for its manifestation. If individuals with ASD are less able to understand and communicate their internal experiences, this has important implications for the efficacy of self-report methods with this population.

These inherent conflicts beg the question of whether self-report and interview techniques represent the most appropriate means of accessing depressive symptoms in the ASD population. Furthermore, while caregiver report represents a viable alternative (Fung, Lunsky and Weiss, 2015), its utility is hampered by a lack of concordance with other measures (Moss et al., 2015).

Phenotypic overlap represents a further challenge to the accurate diagnosis of co-morbid depression, with classic characteristics of ASD often resembling or masking cardinal symptoms of MDD (Magnuson and Constantino, 2011). Low mood (Mazzone et al., 2013), social anhedonia (Chevallier et al., 2012), sleep disturbance (Goldman et al., 2012), monotonous voice (Ghaziuddin and Zafar, 2008), lethargy (Zeina et al., 2014) and flat, restricted affect (Stagg et al., 2014) all constitute examples of MDD diagnostic criteria (APA, 2013) commonly observed in individuals with Autism Spectrum Disorder and no co-occurring depression. Overlap of this magnitude creates a convoluted clinical picture, making it difficult to pinpoint the boundary between the two disorders.

Diagnosing Depression in ASD – Theoretical Difficulties

People with ASD have very different minds (Happé, 2015). It has therefore been postulated that the social, cognitive and communicative features defining the disorder may not only complicate the clinical presentation of depression, but could in fact change it altogether (Matheis and Turygin, 2016).

The notion that different populations may display distinctive symptomatic expressions of depression is not new – with the DSM-IV-TR recognising the possible absence of depressed mood in children with MDD, replaced instead with irritability (APA, 1994). Similarly, the phenomenology of depression in older adults appears to differ; with greater incidence of agitation and hypochondria, and less guilt compared to younger age groups (Hegeman et al., 2012). More pertinently, Tourette syndrome represents another neurodevelopmental disorder that has been associated with atypical presentations of depression, with Piedad and Cavanna (2016) identifying a more irritable phenotype in this population compared to controls. Given the distinctive clinical features of ASD, elucidation of MDD manifestation in this unique population represents an important research objective.

While a number of archetypal symptoms such as tearfulness (Chandrasekhar and Sikich, 2015), low mood (Stewart et al., 2006) and anhedonia (Tandon, Cardeli and Luby, 2009) are detected in ASD populations with depression, many examples of atypical symptomology have also been noted in the literature. For example, Mazzone et al. (2013) observed that individuals with ASD demonstrated externalising symptoms of depression, whereas controls did not. Furthermore, Turygin et al. (2013) found that destructive behaviour was predictive of depression in intellectually impaired adults with ASD, supporting the deduction that increased levels of aggression may represent depression in ASD (Storch et al., 2013). In fact, Chandrasekhar and Sikich (2015) argue that externalising symptoms may supersede internalising indications in this population.

Further evidence for atypical manifestations of depression in ASD comes from the finding that agitation was by far the most common symptom in depressed samples with ASD who had attempted suicide (Takara and Kondo 2014). Chandrasekhar and Sikich’s (2015) case reports echo this finding, with irritability and agitated mood present in both fully and minimally verbal individuals with co-morbid depression. While classic symptoms of depression such as withdrawal, difficulty sleeping and changes to eating habits were present, their case studies also revealed atypical symptoms such as confusion, aggression and unpredictability.

Research also suggests that depression may manifest as changes to the symptom profile of ASD itself. Fluctuation in the frequency of behaviour patterns represents a common theme, with Ozinci, Kahn and Antar (2012) noting an exacerbation in repetitive behaviour in ASD patients with co-occurring depression. Conversely, both Mazzone, Ruta and Reale (2012) and De-la-Iglesia and Olivar, (2015) detected a lack of interest in usual ritualistic behaviour, with the former observing a sudden reduction in stereotypic and obsessive behavioural patterns. Accordingly, Ameis and Szatmari (2015) postulate that anhedonia may masquerade as a decrease in the severity of repetitive behaviour in individuals with autism spectrum disorder. Furthermore, regression of previously learnt skills (Magnuson and Constantino, 2011) and an increase in self-injurious behaviour (Stewart et al., 2006) have also been noted in the literature.

Collation of this research appears to suggest a number of things. First, numerous behavioural manifestations of depression in the ASD population may currently remain diagnostically untapped. Secondly, unexpected changes in observable behaviour and level of functioning from baseline may provide a key diagnostic clue to identifying co-morbid depression in ASD.

Given the vastly heterogenetic nature of ASD presentation, discovery of an archetypal depression phenotype in ASD is unrealistic and unlikely. However, little systematic investigation has been dedicated to identifying the specific ways in which the disorder may manifest differently in this unique population. The possibility of depression presenting atypically in ASD represents an essential theoretical consideration – if people with ASD present with symptom profiles distinct from neuro-typical individuals, it implies that traditional measures of depression diagnosis may not be suitable for use in people with autism spectrum disorder. This is particularly concerning given that the validity of current diagnostic tools has generally not been tested in ASD populations (Magnuson and Constantino 2011).

Reported Differences in Prevalence across the Spectrum – Accurate or an Artefact?

The vast heterogeneity of ASD represents another important challenge to the accurate diagnosis of depression – there are inherent difficulties associated with applying the same diagnostic tools across a population with such phenotypic variation.

A substantial body of research has identified significant differences in prevalence across the spectrum, such that less phenotypically severe individuals appear to incur a significantly greater susceptibility to depression. This pattern dominates throughout the literature, with lower severity of ASD symptoms (Mazurek and Kanne, 2010), higher IQ (Mayes et al., 2011) and higher language abilities (Gotham, Unruh and Lord, 2014) all predicting greater levels of depression. Most notably, it is well established that higher functioning individuals (described as those diagnosed with ASD in the absence of cognitive disability - Hammond and Hoffman, 2014) seem to incur the greatest risk of co-morbid depression (Greenlee et al., 2016).

This disparity in prevalence levels has been described as a product of the enhanced insight, understanding and introspective skills individuals with higher functioning ASD demonstrate compared to their lower functioning counterparts (Magnuson and Constantino, 2011). It is argued that greater self-awareness of functional difficulties (Baron-Cohen, 2008) teamed with a higher expectation of integrating with peers (Chandrasekhar and Sikich 2015) translate into a greater risk of depression. This contention is supported by the finding that greater self-insight of impairment is predictive of higher levels of depression in ASD populations (Vickerstaff et al., 2007).

However, while explanations of this nature may play an important role in understanding the interaction between phenotypic severity of ASD and subsequent risk of co-morbid depression, it is well-documented that the aetiology of MDD also involves a complex interplay of genetic, biochemical and environmental factors (Verduijn et al., 2015) – prevalence explanations with an exclusively cognitive or socio-psychological basis may therefore prove over-simplistic. Consistent detection of greater rates of depressive symptoms in higher functioning individuals (Greenlee et al., 2016) has fuelled the assumption that depression is rare in lower functioning populations. However, a number of studies challenging this rationale have emerged in the literature – with Simonoff et al. (2012), Strang et al. (2012) and Gotham, Unruh and Lord (2015) all reporting no association between IQ and level of depressive symptomology in ASD individuals. Accordingly, Mazzone et al. (2013) found that IQ did not predict severity of MDD symptoms in a sample with ASD. Moyes et al. (2011) even detected a reversal of this widely accepted pattern, reporting increasing levels of depression in more phenotypically severe cases of ASD.

While groups with intellectual disability were historically considered immune to depression (Scott and Havercamp, 2015), today there is little evidence that MDD spares any adult sub-populations with neurodevelopmental disorders (King, 2016). For example, research suggests that groups with intellectual disability (Einfield, Ellis and Emerson, 2011) and Down syndrome (Walker et al., 2011) experience rates of depression comparable to the general population. As such, it has been postulated that previously reported prevalence disparities may better reflect limitations of current diagnostic methodologies (Scott and Havercamp, 2015). Accordingly, evidence that the manifestation of depression in ASD may differ according to the form and severity of an individual’s impairments is beginning to accumulate. For example, Matson and Sturmey (2011) detected differences between depressive symptomology according to cognitive functioning – with lower functioning individuals exhibiting behavioural symptoms to a much greater extent than their higher functioning counterparts. Evidence of this nature suggests that traditional diagnostic tools may serve some sub-populations with ASD better than others.

Given the introspective, communicative and linguistic requirements necessitated by self-report and semi-structured interview techniques (Greenlee et al., 2016), it follows that higher functioning individuals and those without language impairment may be better suited to communicate depressive symptomology in this manner. Their inherent reliance on verbal capacities may render diagnostic tools of this nature differentially valid for use in the ASD population – with more intellectually and verbally proficient individuals better able to express classically described internalising symptoms of depression (Buck et al., 2014), and therefore subsequently more likely to obtain a diagnosis. If this is true, it follows that reported disparities in prevalence may in fact represent poor spectrum-wide sensitivity of diagnostic instruments, as opposed to real differences in susceptibility to depression in ASD.

As such, the phenotypic heterogeneity of ASD represents an important consideration when assessing the validity of current diagnostic tools. Lower functioning and language-impaired individuals with depressive symptoms are particularly at risk of going undetected by current diagnostic techniques. The finding that less verbal (Gotham, Unruh and Lord, 2014) and intellectually impaired (Buck et al., 2014) individuals are less likely to have been diagnosed with depression appears to follow this precedent. Higher functioning individuals are substantially better able to provide valid information relating to their internal experiences compared to those with lower intellectual ability (Pouw et al., 2013), making clinicians reluctant to diagnose psychiatric conditions in lower functioning subgroups (Helverschou, Bakken and Martinsen, 2011). This lends itself to the idea that depression is currently under-diagnosed across the ASD population (Mosley et al., 2011), specifically in lower functioning individuals.

**Conclusion**

The vast phenotypic diversity of ASD teamed with the likely possibility of untapped atypical depressive symptoms in this population suggest that current diagnostic tools may be of limited value for use with individuals diagnosed with autism spectrum disorder. More pressingly, these complications highlight the critical need for current conceptualisations of depression in ASD to be updated.

Better understanding of the distinctive symptom profile of MDD in individuals with ASD represents an important undertaking if the sensitivity of diagnostic tools is to be improved to account for the full scope of ASD presentation. Reports of exceptionally low depression prevalence rates in lower functioning and verbally impaired populations imply that a specific research focus on phenotypically severe sub-groups with ASD represents a valuable enterprise.

The assumption that lower functioning individuals do not experience depression has fuelled a profound lack of research investigating the presentation of depression in individuals with markedly limited social, cognitive and communicative skills. In fact, Magnuson and Constantino (2011) noted a complete absence of studies examining depressive symptomology in lower functioning populations with an IQ below 70. While it remains possible that higher functioning sub-groups incur a comparatively greater risk of depression relative to their lower functioning counterparts, depression is a complex manifestation of a number of interacting aetiological pathways (Fasick et al., 2015). As such, it is unlikely that the severity of ASD symptoms represents the only explanatory factor mediating the relationship between ASD and risk of depression. As such, the widely reported prevalence disparities may represent limitations in existing knowledge of depression presentation (Scott and Havercamp, 2015) as opposed to real differences in disease incidence.

ASD represents an immensely heterogenetic clinical category – making uniform presentation of depression in this population both unrealistic and unlikely. However, by better understanding the intimate interaction between ASD phenotype and depressive symptom profiles, the field moves closer towards the eventual goal of personalised medicine. There is a fundamental demand for research ascertaining the ways in which depression may manifest atypically across the spectrum. This venture has been complicated by the seismic DSM-5 changes to the classification of ASD, and the field must adapt to respond to this. Prior to the paradigm shift, a substantial pool of literature examining differences in the prevalence and presentation of depression between different sub-groups of ASD such as Asperger syndrome, High Functioning Autism and Autistic Disorder had accumulated (e.g. Mukaddes, Hergüner and Tanidir, 2010). With comparisons between these discrete diagnostic categories now effectively redundant, there is a pressing need for research investigating differences in depression manifestation between sub-groups with different impairments and severities as defined by DSM-5’s dimensional model. The notion that there may be differing susceptibility to depression across these groups is supported by Stratis and Lecavalier’s (2013) finding that greater levels of repetitive behaviour and restrictive interests appear to be protective against depression in individuals with ASD.

In sum, there has been a surge in evidence indicating the existence of atypical behavioural manifestations of depression in populations with ASD. This, combined with the inherent shortcomings of self-report and semi-structured interview techniques imply that the apparent absence of archetypal symptoms of depression may not necessarily symbolise the absence of a depressive state in an individual with ASD. Current diagnostic methodology must therefore be adapted to incorporate this.

Research in this field is intrinsically muddied by the fact that the etiology and presentation of both MDD and ASD remain clouded by complexity, controversy and a lack of clarity. However, our knowledge of depression in autism spectrum disorder is particularly obstructed by the profound lack of diagnostic methods validated for use with this very specific population (Mazefsky and White, 2014). Current tools were designed with a neuro-typical population in mind (Mazzone et al., 2013), and therefore do not account for the unique symptomology and phenotypic heterogeneity intrinsic to ASD. Elucidation of the ways in which depressive symptoms may manifest differently across the spectrum paves the way for the development of a separate diagnostic framework tailored to identifying depression in the ASD population. Given the obvious complexity of this task, (Matson and Williams, 2014), a specialised diagnostic instrument is advised.

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