



Review article

Neuropsychological functioning in adolescents and young adults with major depressive disorder – A review

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ABSTRACT

While neuropsychological dysfunction is a contributor to major depressive disorder (MDD) in adult MDD, little is known about neuropsychological function in MDD during adolescence and early adulthood. The aim of this review is to evaluate literature on neuropsychological function in this young age group. A database search of Medline, the Cochrane database and PsycInfo was conducted. Inclusion/exclusion criteria yielded seven case-control studies on neuropsychological functioning in MDD (12–25 years of age) published since 1995. Effect sizes were calculated. Results show a broader range of statistically significant neuropsychological deficits in MDD compared to controls in the cognitive domains of executive function (EF), working memory (WM), psychomotor and processing speed (PPS), verbal fluency (VF) and visual (–spatial) memory (VM). Most convincingly, three out of four studies investigating WM and three out of four studies investigating PPS found statistically significant impairments in MDD with varying effect sizes. EF deficits were reported only in three out of seven studies with small, medium and large effect sizes. While some evidence was found for impaired VM and VF, no evidence was observed for attention and verbal learning and memory; however, these domains have been less extensively studied. Further research is required to broaden the study base.

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1. Introduction

Neuropsychological dysfunction in depression has been researched for more than 50 years and is regarded as a

characteristic of depression indicating a broad profile of affected neuropsychological domains such as memory, concentration and decision-making (Madden et al., 1952; Kiloh and Ball, 1961). Studies in adults and elderly samples have demonstrated that depression is associated with a variety of neuropsychological impairments (Purcell et al., 1997; Austin et al., 2001; Fossati, 2002; Porter et al., 2003, 2007; Fossati et al., 2004; Harvey et al., 2004) such as in executive functioning, attention, memory, and

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psychomotor skills (Sobin and Sackeim, 1997; Fossati et al., 1999, 2004; Airaksinen et al., 2004; Gohier et al., 2009; Baune et al., 2010). In contrast, findings regarding the extent of impairments on neuropsychological tasks in samples of younger adults (21–38 years) with mild to moderate depression have been controversial suggesting a lack of such deficits in younger adults (Grant et al., 2001; Wang et al., 2006; Casteneda et al., 2008). However, limited data has been published in the even younger age groups such as adolescence and early adulthood.

Although the most consistently reported findings of neuropsychological impairments across age groups from younger adults to elderly include executive functioning (Purcell et al., 1997; Fossati et al., 1999; Grant et al., 2001; Harvey et al., 2004; Hill et al., 2004; Stordal et al., 2004; Smith and Muir, 2006; Taylor Tavares et al., 2007; Gohier et al., 2009), adult studies provide evidence to suggest that depression is associated with global cognitive deficits affecting various neuropsychological domains (Gualtieri et al., 2006).

In contrast, there is a paucity of research about the potential impact of depression on neuropsychological functioning in people during early adulthood and adolescence exposed to depression. This is important to note the consequences of early-onset depression are often more severe, far-reaching and show more frequent depressive episodes, possibly causing long-term social and mental disability as compared to later onset of depression in adulthood (Klein et al., 1999; Parker et al., 2003; Gollan et al., 2005a). In addition, research has shown that the psychological, social, physical and biological alterations occurring during adolescence are significant risk factors for the development of depression in young age groups, with a clear increase in prevalence from age 13 years onwards (Abela and Hakin, 2008; Lack and Green, 2009). Despite the prevalence of depression in adolescents and young adults being estimated similar to adults with 5.3% for a 12-month episode and 13.2% for a lifetime major depressive disorder (MDD) (Hasin et al., 2005), depressed young people are more likely to experience recurrent episodes of depression with increased likelihood of suicide, achieve lower educational attainment, and have a higher chance of unemployment and an increased risk of co-morbidities in adulthood (Berndt et al., 2000; Parker et al., 2003; Gollan et al., 2005b; Calles, 2007), which taken together, potentially result in severe long-term psychosocial impairment (Weissman et al., 1999; Dunn and Goodyer, 2006). Given this significant long-term impact of depression at early onset on various outcomes, it is important to better understand the nature of neuropsychological function and dysfunction in this younger age group.

Furthermore, since adult studies suggest a possible relevant functional relationship between neuropsychological function, employment status (Baune et al., 2010) and general function (Airaksinen et al., 2006; Jaeger et al., 2006) in depression, a better clinical description of neuropsychological function and dysfunction in young people with depression would be an important step forward to understand poor outcomes and help identify targets for intervention in depression. Moreover, whether adolescents and young adults are also prone to global cognitive deficits or are better characterised by domain-specific cognitive disturbance remains unclear, although some first evidence suggests domain-specific deficits such as in executive and working memory functioning (Baune et al., 2012) and executive functioning in younger depressed individuals with early onset of depression (Castaneda et al., 2008). Furthermore, studies in adults suggest that cognitive function may be present in a first episode of MDD (indicative of an early sign of MDD) (Lee et al., 2012) and may still be impaired at least in some domains of cognitive function during remission of depression (Hammar and Ardal, 2009) and importantly, that cognitive dysfunction may have a role as a prognostic marker of depression (Reppermund et al., 2009). These clinical observations

on both cause and effects of cognitive dysfunction in depression are highly important for clinical prevention and are unknown in the younger age groups. The identification and treatment of cognitive deficits in depression may help both in improving clinical outcomes and possibly in identifying early signs of deterioration of mood states.

Since these clinical observations demonstrate a need to focus on neuropsychological function in younger age groups, namely adolescents and early adults, it is necessary to frame the review in a context of normative and disruptive brain developmental. The effects of depression in neuropsychological function may depend on the following briefly described important principles of brain development. First, while the developmental trajectory of grey matter (GM) volume follows an inverted U-shape, white matter (WM) volume increases steadily throughout childhood and adolescence and is likely to reflect improved connectivity and integration of disparate neural circuits (Giedd et al., 1999; Lee et al., 2012) and possibly influencing cognitive abilities (Tamnes et al., 2010). With various brain regions undergoing different patterns of maturation, neural consequences of stress-related conditions such as depression depend on the developmental stage at which the stress and depression occurred (Reppermund et al., 2009). Therefore, stress and stress-related depression may have a greater impact on cognitive and emotional function in childhood and adolescence as the brain experiences critical changes compared to adulthood.

Second, since it has been reported that higher-order association cortices develop only after lower-order sensorimotor cortices have matured in structure and function with the frontal lobe structures (e.g. dorsolateral prefrontal cortex (DLPFC)) involved in executive functioning, attention, motor coordination as well as heteromodal association regions the last areas to develop, it has been suggested that complex functions in higher-order structures are more susceptible to the effects of stress-related conditions including depression due to protracted earlier periods of postnatal development (Hammar and Ardal, 2009). Third, genetic and gender influences jointly contribute to individual differences in brain development. Based on these principles of normative brain development, it can be hypothesised that a pathological brain condition such as depression and related stressful experiences impact on neuropsychological function specifically in younger age groups during development.

In summary, given (a) the reported functional implications of neuropsychological deficits in depression, (b) the proposed differences in neuropsychological deficits between young age groups, older adulthood and the elderly, (c) the likely impact of depression on neuropsychological function during adolescence and younger adulthood, and (d) the above mentioned neurobiological normative developmental processes relevant to adolescence and young adulthood (e.g., brain maturation and PFC development), this review focuses on studies in this particular age group.

In this review we evaluate a range of cognitive domains of neuropsychological function as published in the original studies. These include the domains of executive functioning, verbal learning and memory, working memory, visual memory, attention and psychomotor speed. The method and the results sections will define the domains and list the individual cognitive test under each domain for review. In summary, the aim of this review is to characterise a variety of domains of neuropsychological function in depression among individuals between adolescence and young adulthood (12–25 years of age).

2. Methods

A literature search was performed using MEDLINE, the Cochrane Library, and PsycINFO databases covering publications from 1995 to 2014. The following

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