

Lam RW, Kennedy SH, McIntyre RS, et al. Cognitive dysfunction in major depressive disorder: effects on psychosocial functioning and implications for treatment. *Can J Psychiatry*. 2014;59(12):639–648.

Table 1. Summary of primary articles evaluating the associations between psychosocial functioning and cognition, and between antidepressant treatment and cognitive outcomes in MDD (listed in chronological order).

Reference	Subjects	Age (yr)	Gender (% F)	Baseline HAM-D-17 / MADRS	Study design	Outcomes
<i>Associations between psychosocial functioning and cognition</i>						
McCall and Dunn, 2003 ⁶²	77 inpatients with severe MDD, prior to ECT	56.7 ± 15.8	64	28.9 ± 5.0	Cross-sectional study	Global cognition score correlated with activities of daily living.
Jaeger et al, 2006 Error! Bookmark not defined.	48 inpatients with MDD	39.6 ± 12.7	67	16.5 ± 7.1	6-month prospective study	Objective measures of non-verbal, learning, and motor at baseline predicted functional outcomes at 6 months.
Naismith et al, 2007 Error! Bookmark not defined.	21 patients with MDD and matched controls	53.9 ± 11.8	76	21.7 ± 4.4	Cross-sectional study	Self-rated cognitive deficits and objectively-measured psychomotor function predicted physical disability.

Buist-Bouwman et al, 2008 ^{Error!} Bookmark not defined.	21,425 adults; 847 (4.0%) reported MDD episode in last 12 months	-	-	-	Cross-sectional study	Strong association between MDD and psychosocial function. Concentration, attention, and embarrassment mediated the relationship between MDD and function.
Withall et al, 2009 ⁶³	48 inpatients with MDD	38.0 ± 10.6	67	28.3 ± 5.7 at baseline; 10.7 ± 6.0 at follow up	4 month prospective study	Deficits in several neurocognitive domains predicted functional outcome at 4 months followup.
Baune et al, 2010 ^{Error!} Bookmark not defined.	26 outpatients, current MDD	46.0 ± 12.1	27	18.0 ± 5.9	Cross-sectional study	Current MDD = lower cognition scores in all domains vs. healthy controls, and in visuo-spatial /constructional and attention vs. previous MDD. Previous MDD = lower score in immediate memory and attention vs. healthy controls. Employment status was associated with deficits in cognition scores.
	44 patients with previous MDD	44.2 ± 15.9	73	6.8 ± 4.3		
Godard et al, 2011 ⁶⁴	16 outpatients with MDD	49.5 ± 12.3	81	31.2 ± 5.1 (29-item)	Cross-sectional study	Significant correlations between neuropsychological deficits and functional impairment.
<i>Associations between antidepressant treatment and cognitive outcomes</i>						

Reference	Subjects	Age (yr)	Gender (% F)	Baseline HAM-D-17 / MADRS	# of episodes	Study design	Cognitive outcomes
Meyers et al, 1991 Error! Bookmark not defined.	9 patients with MDD treated with nortriptyline	73.4 ± 8	-	Nortriptyline: 5.0 ± 3 Placebo : 6.7 ± 3	-	Cross-over design. 8-26 weeks of nortriptyline followed by 1 week of placebo	Nortriptyline worsened immediate, but not delayed, free recall. No difference between placebo and nortriptyline on measures of immediate and delayed recognition memory.
Constant et al, 2005 Error! Bookmark not defined.	20 outpatients with MDD treated with sertraline and matched controls	47.7 (range: 21-74)	60	Baseline BDI: 25.6 ± 8.0	1 st or 2 nd MDE	7-week prospective study	Patients with MDD: disturbances in attention, executive, and psychomotor function vs. controls. Sertraline improved attention, executive, and psychomotor function.
Ferguson et al, 2003 Error! Bookmark not defined.	25 patients with MDD treated with reboxetine	Range: 18-65, as per design	-	>20, as per design	-	Two 8-week, placebo-controlled, double-blind RCTs	Reboxetine: improved sustained attention and cognitive functioning speed at day 56 vs. baseline. Paroxetine and placebo: no significant effect on
	23 patients with MDD treated with paroxetine		-		-		

	74 patients with MDD treated with placebo		-		-		these cognitive endpoints.
Gualtieri et al, 2007 Error! Bookmark not defined.	27 outpatients with MDD treated with SSRI	43.8	59	-	-	Cross-sectional study	SSRI patients: scored lower on psychomotor speed, cognitive flexibility, and reaction time vs. matched controls. Venlafaxine patients: scored lower on reaction test during a Stroop test vs. matched controls. Bupropion patients: did not differ from matched controls in any cognitive domain.
	27 outpatients with MDD treated with venlafaxine	46.1	59	-	-		
	27 outpatients with MDD treated with bupropion	44.0	74	-	-		
	27 matched controls	43.8	63	-	-		
Raskin et al, 2007 Error! Bookmark	207 outpatients with MDD treated with duloxetine	72.6 ± 5.7	60	22.4 ± 3.8	5.0 ± 15.0	8-week placebo-controlled, double-blind RCT	Duloxetine: significant improvement in composite cognitive score vs. placebo (improvement mainly

not defined.	104 outpatients with MDD treated with placebo	73.3 ± 5.7	58	22.0 ± 3.6	6.3 ± 13.6		driven by verbal learning and memory).
Herrera-Guzman et al, 2008 Error! Bookmark not defined.	20 outpatients with MDD treated with bupropion	24.5 ± 4.7	92	Responders: 26.8 ± 6.1 Non-responders: 21.8 ± 3.3	5.3 ± 5.5	8-week clinical trial	Low pretreatment visual memory and processing speed were predictive of good response to bupropion. Visual memory and processing speed improved during treatment.
Culang et al, 2009 Error! Bookmark not defined.	84 outpatients with MDD treated with citalopram	79.8 ± 4.0	54	24.4 ± 4.3	-	8-week double-blind, placebo-controlled RCT	Citalopram responders: improved in visuospatial functioning vs. non-responders, but not vs. placebo responders. Citalopram responders: improved in psychomotor speed vs. citalopram non-responders, but not vs. placebo.
	90 outpatients with MDD treated with placebo	79.3 ± 4.7	62	24.3 ± 3.9	-		
Herrera-Guzman et al,	36 patients with MDD treated with escitalopram	32.9 ± 8.7	86.1	25.3 ± 4.0	3.8 ± 4.8	24-week clinical trial	Both treatments improved episodic memory, working memory, mental

2009 Error! Bookmark not defined.	37 patients with MDD treated with duloxetine	33.2 ± 8.6	75.7	25.1 ± 5.3	3.6 ± 3.5		processing speed and motor performance. Duloxetine was more effective than escitalopram at improving episodic and working memory.
Herrera-Guzman et al, 2010 Error! Bookmark not defined.	36 patients with MDD previously treated with escitalopram	32.9 ± 8.7	86.1	25.3 ± 4.0	3.8 ± 4.8	24-week follow-up after cessation of medication	Patients with remitted MDD performed worse on verbal and visual memory, attention, and working memory vs. healthy controls. Patients previously treated with a SNRI performed better in episodic visual and verbal memory vs. patients previously treated with a SSRI.
	37 patients with MDD previously treated with duloxetine	33.2 ± 8.6	75.7	25.1 ± 5.3	3.6 ± 3.5		
Culang-Reinlieb et al, 2012 Error! Bookmark not defined.	33 patients with MDD treated with sertraline	64.9 ± 8.8	61	23.9 ± 4.4	-	12-week clinical trial	Sertraline patients: improved more on verbal learning vs. nortriptyline
	30 patients with MDD treated with nortriptyline	63.5 ± 8.2	60	24.9 ± 5.4	-		

Katona et al, 2012 Error! Bookmark not defined.	156 elderly patients with MDD treated with vortioxetine	70.5 ± 4.8	69	22.7 ± 3.9	-	8-week double-blind, randomized, placebo- and active-controlled trial	Vortioxetine (LU AA21004), but not duloxetine, improved speed of processing, verbal learning and memory vs. placebo
	151 elderly patients with MDD treated with duloxetine	70.9 ± 5.5	66	22.3 ± 3.9	-		
	145 elderly patients with MDD treated with placebo	70.3 ± 4.4	62	22.7 ± 3.9	-		
McIntyre et al, 2014 Error! Bookmark not defined.	195 MDD outpatients treated with vortioxetine 10 mg/d	45.4 ± 12.2	69	31.6 ± 3.8	2.3 ± 1.7	8-week multinational, double-blind, randomized, placebo-controlled trial	Vortioxetine 10 and 20 mg/d significantly improved a composite of cognitive measures (DSST and RAVLT) vs. placebo
	207 MDD outpatients treated with vortioxetine 10 mg/d	46.1 ± 11.8	64	31.7 ± 3.5	2.6 ± 2.1		Patient-reported cognition was also significantly improved with vortioxetine vs. placebo.

196 MDD outpatients treated with placebo	45.6 ± 12.1	66	31.3 ± 3.8	2.4 ± 2.0	
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Data are presented as mean ± SD unless otherwise noted. '-' denotes that data were not available. BDI: Beck Depression Index; F: females; HAM-D-17: 17-item Hamilton depression scale; MADRS: Montgomery-Asberg Depression Rating Scale; MDD: major depressive disorder; SD: standard deviation; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; RCT: randomized controlled trial; MDE: major depressive episode; DSST: digit symbol substitution test; RAVLT: Ray auditory verbal learning test.