



**CLINICAL TRIALS IN WHICH
THE CDR SYSTEM HAS BEEN USED
TO DETECT ENHANCEMENTS IN COGNITIVE FUNCTION**

190 clinical trials conducted from 1975 to the present

Described in:

**147 peer-reviewed publications
37 published conference abstracts
4 unpublished conference abstracts**

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Data from:

- **5,795 Healthy volunteers**
 - 1,647 - Aged 5 to 17 years
 - 2,726 - Aged 18 to 40 years
 - 986 - Aged 40 to 65 years
 - 436 - Aged 65 and above
- **8,778 patients from 33 different clinical conditions**
 - Age Associated Memory Impairment (AAMI)
 - Alzheimer's disease (AD)
 - ADHD both Childhood & Adult
 - Coronary Artery Bypass Graft Patients (CABG)
 - Carotid Endarterectomy Patients
 - Chronic Fatigue Syndrome (CFS)
 - Cocaine Dependents
 - Dental Anxiety Patients
 - Dementia with Lewy bodies (DLB)
 - Epilepsy
 - Fibromyalgia
 - Hepatic Encephalopathy
 - Hypertension
 - Kidney dialysis Patients
 - Mild-Cognitive Impairment (MCI)
 - Major Depressive Disorder (MDD)
 - Narcolepsy
 - Neurasthenia
 - Oncology – Breast cancer, Haematological disorders & Terminal
 - Parkinson's disease
 - Patients with Reduced Cardio-Vascular Reserve
 - Parkinson's disease dementia (PDD)
 - Post-Operative Cognitive Decline (POCD)
 - Post-Menopausal Females
 - Recreational Drug Users
 - Shift-Work Sleep Disorder
 - Sleep Apnoea
 - Stimulant Abusers
 - Stroke
 - Urology

Statistically reliable cognition enhancement was found in one or more of the domains of cognitive function assessed in 180 of the 188 studies

ANTICHOLINESTERASES

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/LTM	Ref
Donepezil 10 mg	Young Vols	23	Scopolamine Model	↑	↑	↑	55
Donepezil 5 mg	Young Vols	20	Scopolamine Model	↑	↑	↑	57
Donepezil 10 mg	Elderly Vols	12	Scopolamine Model	↑	↑	↑	20
Physostigmine 0.5, 1 & 2 mg sc	Young Vols	10	Scopolamine Model	↑	↑	↑	19
Physostigmine 2 mg sc	Young Vols	24	Scopolamine Model	↑	↑	↑	145
Physostigmine 2 mg iv	Young Vols	12	x-over single dose	↑	↔	↑	144
Physostigmine	AD	12	x-over single dose			↑	96
Tacrine	AD	24	x-over 12-weeks	↑	↔	↑	115
Velnacrine	Young Vols	31	Scopolamine Model	↔	↔	↑	97
Velnacrine	AD	12	x-over single dose			↑	96
Velnacrine	AD	35	x-over 10 days	↑	↔	↑	30,96
ZT-1 Huperzine A	Elderly Vols	10	Scopolamine Model	↑	↑	↑	152, 157
Galantamine	AD	18	x-over 12-weeks	↑	↔	↔	115
Galantamine	AD	30	Randomised 6 months	↑			116
Galantamine	AD MMSE 12-24	58	// group 8 weeks	↑			26
Galantamine	AD MMSE 5-22	80	// group 12 months	↑			26
Galantamine	AD MMSE 16-26	373	Open Label 12 weeks	↑			109
Donepezil 5 to 10 mg	DLB MMSE 10-24	22	20 weeks open label	↑			86
Donepezil 5 to 10 mg	PDD MMSE 10-24	23	20 weeks open label	↑			86
Rivastigmine	DLB MMSE 10-25	120	// group 23 weeks	↑	↑	↑	60,131
Rivastigmine	DLB hallucinators	71	// group 23 weeks	↑	↔	↔	61
Rivastigmine	DLB gene for BuChE	55	// group 20 weeks	↑			10,73
Rivastigmine	PDD MMSE 10-24	541	// group 6 months	↑			22,81,104, 119,130
Rivastigmine	PDD homocysteinemia	260	// group 6 months	↑			7
Rivastigmine	PDD hallucinators	298	// group 6 months	↑			11
Rivastigmine	PDD & poor attention	288	// group 6 months	↑			164
Galantamine	Chronic Fatigue	434	// group 4 months	↔	↔	↔	164
Galantamine	Fibromyalgia	71	// group 5 months	↑	↑	↑	146

↑ = statistically significant enhancement ↔ = no significant change ↓ = significant impairment

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PHARMACEUTICAL INDUSTRY DEVELOPED COGNITION ENHANCERS

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/LTM	Ref
Aniracetam 1500 mg	Young Vols	28	Scopolamine Model	↑	↑	↑	4
Aniracetam 1500 mg	Young Vols	26	Scopolamine Model	↑	↑	↑	121
Armodafinil 150 mg	Shift-Work Sleep Disorder	254	// group 12 weeks	↑		↑	14
Armodafinil 150 & 250 mg	Narcolepsy	194	// group 12 weeks	↑		↑	31
Armodafinil 150 mg	Sleep Apnoea	259	// group 12 weeks	↔		↑	36
Armodafinil 150 & 250 mg	Sleep Apnoea	395	// group 12 weeks	↑		↑	85
D-Cycloserine 15 mg	Young Vols	23	Scopolamine Model	↔	↑	↑	125
D-Cycloserine 5 & 15 mg	Elderly Vols	24	Scopolamine Model	↔	↔	↑	40
D-Cycloserine 5 & 15 mg	Elderly Vols	24	x-over single dose	↔	↔	↑	173
D-Cycloserine 5, 15 & 50 mg	AD MMSE 12-27	403	// group 26 weeks	↔	↔	↔	183
D-Cycloserine 5, 15 & 50 mg	AD MMSE 12-24	40	// group 26 weeks	↔	↔	↔	184
E-5842 10 & 20 mg <i>sigma1 ligand</i>	Young Vols	25	// group 7 days	↑	↑	↑	169
FK960 0.2 to 200 mg	Young Vols	10	Scopolamine Model	↑	↑	↑	135
Flesinoxan <i>5HT1A full agonist</i>	Elderly Vols	36	x-over 11 days	↑	↔	↔	117
Lecozotan Silent <i>5HT1A antagonist</i>	Young Vols	20	Scopolamine Model	↔	↔	↔	117
HOE 427 <i>ACTH analogue</i>	AAMI	20	x-over	↑	↑	↔	95
Memantine	DLB & PDD	51	// group 24 weeks	↑		↑	188
Moclobemide <i>MAO-A inhibitor</i>	Young Vols	28	Scopolamine Model	↑	↑	↑	120
Moclobemide <i>MAO-A inhibitor</i>	Young Vols	24	x-over single dose	↓	↔	↑	142
Moclobemide <i>MAO-A inhibitor</i>	Vols 60-75 years	27	x-over single dose	↔	↑	↑	140,141
Moclobemide <i>MAO-A inhibitor</i>	MDD 60-75 years	16	// group 12 weeks	↑	↔	↔	126
Modafinil 200 mg	Young Vols	36	// group single dose	↑	↑		129
Modafinil 200 mg	Breast Cancer	76	// group 8 weeks	↑	↔	↑	53
NS2359 <i>5HT, NE & DA Reup. Inhib</i>	Young Vols	40	single dose	↑	↔	↑	9
NS2359 <i>5HT, NE & DA Reup. Inhib</i>	Adult ADHD	126	single dose	↑	↔	↑	153
NS2330 <i>5HT, NE & DA Reup. Inhib</i>	Young Vols	16	single dose	↑	↑	↔	41
NS2330 <i>5HT, NE & DA Reup. Inhib</i>	Young Vols	32	single dose	↑	↑	↑	156
NS2330 <i>5HT, NE & DA Reup. Inhib</i>	AD MMSE 20-26	32	// group 28 days	↑	↑	↑	114
ORM-12741 alpha-2C adrenoceptor antagonist	AD MMSE 12 to 21	100	// group 12 weeks	↔	↑	↑	187
Piracetam 2400 mg	Young Vols	26	Scopolamine Model	↔	↑	↔	121
S17092 <i>prolyl endopeptidase inhib</i>	Young Vols	36	// group single dose	↑	↔	↑	65
S17092 <i>prolyl endopeptidase inhib</i>	Elderly Vols	36	// group single dose	↔	↑	↑	66
Sibutramine <i>5HT& NE Reup. Inhib</i>	Young Vols	20	x-over single dose	↑	↔	↑	124
SB-202026 <i>muscarinic agonist</i>	Elderly Vols	20	x-over single dose	↑	↔	↔	159
Tenilsetam 150 & 300 mg	Young Vols	18	Scopolamine Model	↑	↑	↑	143
Tenilsetam 150 & 300 mg	Young Vols	18	x-over single dose	↑	↑	↑	143

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NICOTINE AND INDUSTRY DEVELOPED NICOTINIC AGONISTS

Intervention	Population	N	Design	ATT & IP	WM & EF	EM/LTM	Ref
Nicotine – Cigarettes	Young Vols	19	x-over	↑	↑		21
Nicotine – Cigarettes	Young Vols	16	x-over	↑	↑		78
Nicotine – Cigarettes	Young Vols	20	x-over	↑	↑		77
Nicotine – Cigarettes	Young Vols	16	x-over	↑	↑		76
Nicotine – Cigarettes	Young Vols	25	x-over	↑	↑		150
Nicotine – Cigarettes	Young Vols	30	x-over	↑	↑		83
Nicotine – Cigarettes	Young Vols	24	x-over	↑	↑		118
Nicotine – Cigarettes	Young Vols	16	x-over	↑	↑		132
Nicotine – Cigarettes	Young Vols	6	x-over	↑			59
Nicotine – Cigarettes	Young Vols	36	x-over	↑	↑		139
Nicotine – Cigarettes	Young Vols	24	x-over	↑	↑		147
Nicotine – Cigarettes	Young Vols	12	x-over	↑	↑		147
Nicotine – Cigarettes	Young Vols	40	x-over	↑	↑		148
Nicotine – Cigarettes	Young Vols	16	x-over	↑	↑		128
Nicotine – Cigarettes	Young Vols	30	x-over	↑	↔	↑	186
Nicotine – Tablets	Young Vols	12	x-over	↑	↑		149
Nicotine – Tablets	Young Vols	16	x-over	↑			136
Nicotine – Tablets	Young Vols	36	x-over	↑			111
Nicotine – Tablets	Young Vols	12	x-over	↑	↑		137
Nicotine – Tablets	Young Vols	12	Scopolamine Model	↑	↑		137
Nicotine – Gum	Young Vols	16	x-over	↑	↑		76
Nicotine – Gum	Young Vols	16	x-over	↑	↑		78
Nicotine – Inhaler	Young Vols	20	x-over	↑	↑		94
Nicotine – Patches	MCI	67	// group 6 m	↑	↑	↑	72
TC-1734/AZ 3480 $\alpha 4\beta 2$ agonist	Young Vols	24	// group 10 d	↑	↔	↑	15,27
TC-1734/AZ 3480 $\alpha 4\beta 2$ agonist	Elderly Vols	8	x-over	↑	↔	↑	16
TC-1734/AZ 3480 $\alpha 4\beta 2$ agonist	AAMI	76	// group 3 weeks	↑	↑	↑	18
TC-1734/AZ 3480 $\alpha 4\beta 2$ agonist	MCI	40	// group 3 weeks	↑	↑	↑	17
ABT-089 $\alpha 4\beta 2$ agonist	Young Vols	18	x-over 4 days	↑	↑	↑	5
ABT-089 $\alpha 4\beta 2$ agonist	Young Vols	18	Scopolamine Model	↑	↑	↑	5
ABT-089 $\alpha 4\beta 2$ agonist	Adult ADHD	11	x-over 2 weeks	↑	↑	↑	154
GTS-21 $\alpha 7$ agonist	Young Vols	18	x-over 5 days	↑	↑	↑	52
MEM3454 $\alpha 7$ agonist 5HT3 antag	Young Vols	48	// group 13 days	↔	↔	↑	12
MEM3454 $\alpha 7$ agonist 5HT3 antag	AD MMSE 12-25	80	// group 8 weeks	↔	↑	↑	160
S-12024 vasopressin agonist	AD MMSE 10-23	53	// group 28 days	↑		↑	1
S-12024 vasopressin agonist	Elderly Vols	36	// group 8 days	↔	↑	↑	113

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STIMULANTS

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/ LTM	Ref
d-amphetamine 0.42mg/kg	Stimulant abusers	20	x-over single dose	↑			98
d-methamphetamine 0.42 mg/kg	Stimulant abusers	20	x-over single dose	↑			98
d-methamphetamine 0.42 mg/kg	Recreational drug users	61	x-over, single dose	↑	↔		100
d,l-methamphetamine 0.42mg/kg	Stimulant abusers	20	x-over single dose	↑			98
Cocaine i.v.	Cocaine dependents	12	x-over 23 days	↑			67
Cocaine smoked	Cocaine dependents	17	x-over 21 days	↑	↔	↑	74
Cocaine smoked	Cocaine dependents	5	x-over 21 days	↑	↔	↑	75

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PHARMACEUTICALS WHICH IMPROVE COGNITIVE FUNCTION

Intervention	Population	N	Design	ATT & IP	WM & EF	EM/LTM	Ref
Flumazenil oral	Dental anxiety	25	x-over Midazolam reversal	↑	↑	↑	29
Flumazenil iv	Dental anxiety	18	x-over Midazolam reversal	↔	↑	↑	28
Flumazenil im	Urology	44	Midazolam reversal	↑			8
Amisulpride 50 & 200mg	Elderly Vols	16	x-over single dose	↑	↔	↔	45
Remacemide <i>NMDA ant</i>	Epilepsy 12-75 years	570	// groups 12 months	↑	↔	↑	122
LOLA 9g (L-ornithine L-Aspartate)	Hepatic encephalopathy	43	// group 4 weeks	↔	↔	↑	63
Candesartan	Hypertensives 70-89 years	257	// group 5 years	↑	↔	↑	88
Cilazapril replacement for atenolol	Hypertensives 65+ years	27	// group 20 weeks	↑	↔	↔	35
lanthanum carbonate	Kidney dialysis	360	// group 2 years	↑	↑	↔	2
Desvenlafaxine	MDD 20-65 years	81	// group 12 weeks	↔	↑	↔	82
Paroxetine	MDD 18-65 years	49	// group 8 weeks	↑	↑	↑	24
Reboxetine	MDD 18-65 years	51	// group 8 weeks	↑	↑	↑	24
Levomilnacipran	MDD 18-80 years	442	// group 10 weeks	↑			185
Nortriptyline	MDD 60-75 years	16	// group 12 weeks	↑	↔	↔	126
Moclobemide	MDD 60-75 years	16	// group 12 weeks	↑	↔	↔	126
Epoetin alfa	Oncology Haematologic malignancies	903	// groups 12 weeks	↔	↑	↑	105, 170
Fentanyl (switching from morphine)	Oncology Terminal	19	14 days	↔	↑	↑	62
Estradiol Transdermal	Post-menopausal females 62-89 years	19	// group 12 weeks	↑	↔	↔	89

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NATURAL PRODUCTS WHICH ENHANCE COGNITIVE FUNCTION - I

Caffeine, Guarana, Oxygen & Glucose

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/ LTM	Ref
Caffeine 100 mg	Young Vols	17	x-over	↑			59
Caffeine	Young Vols	30	x-over shift-work mod.	↑			39
Caffeine 150 mg	Young Vols	24	x-over single dose	↑	↑		32
Caffeine 75 & 150 mg	Young Vols non-caffeine users	24	x-over single dose	↑	↑	↔	34
Caffeine 75 & 150 mg	Young Vols caffeine users	24	x-over single dose	↑	↑	↔	34
Caffeine 150mg & L-theanine 250mg	Young Vols	24	x-over single dose	↑	↑	↑	32
Guarana 37.5 & 75 mg	Young Vols	26	x-over single dose	↑	↑	↑	33
Guarana 75 mg	Young Vols	28	x-over single dose	↑	↔	↑	44
Red Bull	Young Vols	24	x-over single dose	↑			165
Energy Drink Caffeine 75 mg & glucose 37.5 g	Young Vols	20	x-over single dose	↑	↔	↑	91
Energy shot – caffeine 140 mg glucose free, B vitamins & amino acids	Young Vols	91	x-over single dose	↑	↑	↑	110
Glucose 40 g	Children 5-6 years	30	x-over acute	↔	↑	↔	103
Glucose 40 g	Young Vols	18	x-over acute	↑	↓	↓	38
Glucose 25 g	Young Vols	20	x-over acute			↑	25
Oxygen	Elderly Vols	20	x-over acute	↑	↔	↑	71
Oxygen	Young Vols	20	x-over acute	↑	↔	↑	72
Oxygen	Young Vols	20	x-over acute			↑	93
Oxygen	Young Vols	32	x-over acute	↑		↑	92
Oxygen	CFS	16	x-over acute	↑		↔	166

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NATURAL PRODUCTS WHICH ENHANCE COGNITIVE FUNCTION - II

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/ LTM	Ref
Bacopa Monniera 300 mg	Vols 18-60 years	107	// group 90 days	↔	↑	↔	99
Breakfast Cereals Low v High GI	Children 6-11 yrs	64	x-over acute	↑	↔	↑	37
Breakfast Cereals	Children 9-16 yrs	29	x-over acute	↑	↔	↑	133
Breakfast	Children 6-16 yrs	1386	// group Internet	↑		↑	134
Breakfast Isomaltulose enriched milk	Children 5-6 years	30	x-over acute	↑	↔	↔	103
Chewing Gum	Young Vols	75	// group	↔	↑	↑	155
Docosahexaenoic Acid (DHA)	Children 10-12 yrs	90	// group 8-weeks	↔	↔	↑↓	182
Docosahexaenoic Acid (DHA)	Elderly Vols	74	// group 90 days	↔	↔	↔	180
Fat 16 g	Young Vols	18	x-over acute	↑	↑	↑	38
Huperzine A, Vinpocetine & Acetyl-L-Carnitine	Vols 22-60 years	74	// group 30 days	↔	↑	↑	101
Melissa Officinalis 300- 900 mg <i>Non-cholinergic binding</i>	Young Vols	20	x-over single dose	↑	↓	↓	46
Melissa Officinalis 600-1600 mg <i>Cholinergic binding</i>	Young Vols	20	x-over single dose	↑	↑	↑	51
Peppermint Essential Oil	Young Vols	96	// group single dose	↔	↑	↑	69
Protein 40 g	Young Vols	18	x-over acute	↔	↑	↑	38
Pycnogenol 150 mg	Vols 60-85 years	101	// group 3 months	↔	↑	↔	87
Rosemary Essential Oil	Young Vols	96	// group single dose	↔	↔	↑	68
Rosemary 100% powder 750 mg	Vols 65-90 years	28	x-over single dose	↔	↓	↑	79
Salvia Officinalis 167 & 333 mg	Vols 65-90 years	20	x-over single dose	↑	↑	↑	90
Salvia Lavandulaefolia 50 & 100 µl	Young Vols	20	x-over single dose			↑	106
Salvia Lavandulaefolia 25 & 50 µl	Young Vols	24	x-over single dose			↑	106
Salvia Lavandulaefolia 25 & 50 µl	Young Vols	24	x-over single dose	↔	↔	↑	107
Water	Dehydrated Young Vols	24	x-over single dose	↔	↔	↔	179

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NATURAL PRODUCTS WHICH ENHANCE COGNITIVE FUNCTION - III

GINKGO BILOBA & GINSENG

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/LTM	Ref
Ginkgo Biloba – Tanakan	MCI	54	// group 12 weeks	↑	↑	↑	138
Ginkgo Biloba – GK501 120 mg	Young Vols	20	x-over single dose	↔	↑	↑	47
Ginkgo Biloba – GK501 120 mg	Young Vols	87	x-over single dose	↓	↑	↑	43
Ginkgo Biloba – GK501 120 mg	Vols 40-60 years	120	// group 8 weeks	↔	↑	↑	112
Ginkgo Biloba – GK501 240&360 mg	Young Vols	20	x-over single dose	↑	↔	↔	47
Ginkgo Biloba – GK501 360 mg	Young Vols	20	x-over single dose	↔	↔	↑	50
Ginkgo Biloba – GK501 120 mg & phosphatidylserine 360 mg	Young Vols	18	x-over single dose	↑	↑	↑	42
Ginkgo Biloba – GK501 120 mg & phostphatidylcholine 360 mg	Young Vols	18	x-over single dose	↔	↔	↑	42
Panax Ginseng G115 200 mg	Young Vols	28	x-over single dose	↑	↑	↑	44
Panax Ginseng G115 200 mg	Young Vols	18	// group 21 days	↑	↑	↑	54
Panax Ginseng G115 200 & 600 mg	Young Vols	20	x-over single dose	↓	↔	↑	49
Panax Ginseng G115 400 mg	Young Vols	20	x-over single dose	↔	↔	↑	49
Panax Ginseng G115 400 mg	Young Vols	20	x-over single dose	↑	↔	↑	50
Panax Ginseng G115 400 mg	Young Vols	30	x-over single dose	↑	↔	↔	102
G115 200 mg & Guarana 75 mg	Young Vols	28	x-over single dose	↑	↔	↑	44
GK501 120 mg & G115 200 mg	Neurasthenia 40-65 years	64	// group 90 Days	↔	↑	↑	123
GK501 120 mg & G115 200 mg	Vols 40-66 years	256	// group 90 Days	↔	↑	↑	151
GK501 360 mg & G115 600 mg	Young Vols	20	x-over single dose	↓	↑	↑	50
GK501 360 mg & G115 600 mg	Young Vols	20	x-over single dose	↔	↑	↑	48
Pharmaton Capsules	Vols 18-75 years	622	Internet Users v Non-Users	↑		↑	161
Pharmaton Capsules	Vols 20-45 years	31	// group 3 months Night Shift Model	↔	↔	↑	127

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INTERVENTIONS WHICH IMPROVE COGNITIVE FUNCTION

Intervention	Population	n	Design	ATT & IP	WM & EF	EM/ LTM	Ref
Altitude -Dropping from 5200 to 3600 metres	Volunteers 18-54 years	25	Cross-over 4 weeks	↑	↔	↔	162
Anaesthesia – Control of depth	POCD & Controls	72	// group 1 Year	↑			6
Carotid Endarterectomy	Patients with reduced CVR	179	// group 8 weeks	↑	↑	↑	23
Cardiopulmonary bypass	CABG 50-85 years	54	Sequential 6 months	↑	↑	↑	108
Cardiopulmonary bypass	CABG 54-86 years	89	// group 6 months	↑	↑	↑	64
Classroom ventilation	Children 10-11 years	18	x-over	↑			13
Deep Brain stimulation of the pedunclopontine nucleus	Parkinson’s Disease	11	x-over 4 frequencies	↑	↔	↔	181
HeartMath Coherence Training	ADHD 9-13 years	35	// group 12 weeks	↔	↔	↑	56
Mobile phone 915-MHz simulated signal	Volunteers 21-60 years	36	x-over acute	↑	↔	↔	80
Liver Transplant	Hepatic Encephalopathy	21	2 to 21 months	↑	↑	↑	58
Recovery from acute stroke – over 1 & 8 weeks	Stroke	12	Repeated measures	↑	↑	↑	163, 173

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