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Table 1: Summary of clinical studies investigating the effect of chronic pain on cognition

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Attention	Numerical interference	Chronic intractable benign pain of lower back, limb or other n=22	VAS, PPI of MPQ, NRS, pain intensity descriptor scale	No significant correlation between numerical interference task performance and pain scores	No association between age, pain chronicity, gender, anxiety, depression, medication or site of pain and cognitive performance. Cognition not affected in low pain subgroup	Eccleston (1994)
Attention	Stroop task	Chronic intractable benign pain of lower back and other n=33	VAS	No correlation analysis performed for cognition and pain ratings	No association between trait-anxiety or depression and cognition, no association between pain and response accuracy	Grisart and Plaghki (1999)
Attention	TEA	Fibromyalgia, rheumatoid arthritis and musculoskeletal pain n=60	VAS	No correlation analysis performed for cognition and pain ratings	Age, depression, anxiety, somatic awareness and catastrophizing were accounted for statistically. Opioid use did not affect TEA performance	Dick et al. (2002)
Attention	Probe task	Chronic low back pain, failed back surgery syndrome, radiculopathy, pain in lower limbs, neuropathy, painful scarring	VAS	No correlation analysis performed for cognition and pain ratings	Chronic pain patients had significantly lower IQ scores than controls on adapted National Adult Reading Test	Veldhuijzen et al. (2006a)
Attention, maintenance of a working memory trace	TEA, spatial span test (mirror task)	Chronic pain of joints back, limbs or other n=24	NRS, MPQ	No correlation analysis performed for cognition and pain ratings	A subset of patients showed no impairment on TEA, no effect of pain on spatial span orientation test or reading span test	Dick and Rashiq (2007)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Attention, working memory, immediate and delayed verbal memory, broad cognitive functioning	Bourdon-Vos test, Digit-span backward test, Story recall subtest of the Rivermead Behavioural Memory Test, MMSE	Chronic visceral, musculoskeletal or neuropathic pain or other (e.g. migraine)	VAS	Significant correlation between working memory performance and pain intensity (r= -0.38, P<0.05)	No association between pain intensity and semantic memory, immediate or delayed verbal memory, or visuospatial memory. Sleep quality and depression did not correlate with cognitive performance. Opioid use and recruitment procedure did not affect task performance. Correlation was significant after adjusting for age	Oosterman et al. (2010)
Immediate verbal memory, delayed memory and sustained concentration	WMS-R, PASAT	Fibromyalgia n=30	MPI-PS	Significant correlation between WMS-R general memory (r= -0.35, p<0.05) and PASAT scores (r= -0.36, p <0.05) and MPI-PS pain scores	No association between pain and auditory verbal learning, visual memory. Anxiety and self-reported cognitive complaints were correlated with cognitive performance	Grace et al. (1999)
Working memory capacity, free recall, and recognition memory	Computer based reading span test, word list recall and recognition tests	Fibromyalgia n=23	MPQ, AIMS pain subscale	Significant correlation between working memory capacity (r= -0.466, p=0.022) free recall (r= -0.607, p=0.002) and recognition memory (r= -0.555, p=0.005) and AIMS pain scores. Significant correlation between free recall (r= -0.441, p=0.031) and MPQ scores	Female subject cohort. No association between pain and information-processing speed or verbal fluency. No association between depression or anxiety and cognitive performance. Self-reported cognitive complaints were correlated with cognitive task performance	Park et al. (2001)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Spatial working and long-term memory	Corsi Block span test, Rey Visual Design Learning test	Fibromyalgia n=20	MPQ, pain experience scale	No significant correlation between Corsi Block span test and Rey Visual Design Learning test performance and pain scores	No association between pain and verbal working or long-term memory, or attention. No association between depression and cognitive performance	Luerding et al. (2008)
Psychomotor efficiency	Grooved pegboard test, Digit vigilance test, Embedded figures test, WAIS-R digit symbol test	Diabetic neuropathy n= 42	Clinical examination	No correlation analysis performed for cognition and pain ratings	No association between pain and spatial processing, verbal intelligence, learning, memory, problem solving, or simple motor speed	Ryan et al. (1992)
Psychomotor efficiency, sustained attention, visual scanning and decision making, mental flexibility	Grooved pegboard test, Digit Vigilance Test, Embedded Figures Test, Trail Making Test	Diabetic neuropathy n=58	Clinical examination	No correlation analysis performed for cognition and pain ratings but diagnosis of neuropathy was correlated with impaired performance on Digit Vigilance Test (r^2= 0.062, p<0.05), Embedded Figures Test (r^2= 0.046, p<0.05), Grooved Pegboard test (r^2=0.087, p<0.05) and Trail Making test (r^2=0.027, p<0.05)	No association between neuropathy and memory	Ryan et al. (1993)
Speed of information processing, attention	P300 latency and amplitude	Fibromyalgia n=34	ACR diagnostic criteria, SF-36 pain subscale	No significant correlation observed between SF-36 pain subscale score and the P300 latency or amplitude	Female subject cohort. No correlation between disease duration or tender point count and P300	Alanoglu et al. (2005)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Psychomotor efficiency	Grooved pegboard test	Diabetic neuropathy n=200	Clinical examination	No correlation analysis performed for cognition and pain ratings but diagnosis of neuropathy was correlated with performance on the Grooved Pegboard test (r and *p* values not quoted)	Retinopathy, vascular disease, nephropathy, coronary artery disease systolic blood pressure and duration of diabetes also affected psychomotor efficiency, no association between pain and problem solving, learning and memory and verbal working memory	Ryan (2005)
Psychomotor efficiency, broad cognitive functioning, immediate and delayed memory, language and metal flexibility	Grooved pegboard test, MMSE, RBANS immediate and delayed memory and language subtests, Trail Making Test	Chronic Low Back Pain n= 163	MPQ-SF	Significant correlation between neuropsychological test scores and MPQ scores (r= -0.17, P<0.001), most strongly between mental flexibility and psychomotor efficiency	Older adult patient cohort. Attention and visuospatial memory were negatively correlated with pain scores but were not significantly impaired in chronic pain patients compared with controls. Depression and presence of comorbidities were not correlated with cognitive performance	Weiner et al. (2006)
Psychomotor efficiency, working memory	WAIS-III digit-symbol test	Undiagnosed chronic widespread pain	ACR diagnostic criteria, number of pain sites	Significant correlation between digit-symbol test performance and pain status (P=0.04), and between digit-symbol test performance and number of pain sites (P=0.048, r values not quoted)	Male patient cohort. No effect of pain on visual memory, visual constructional ability or recognition memory. Age, education, test centre, smoking, frequency alcohol consumption of depression, number of co-morbidities, BMI, physical function and medication affected cognitive performance, but correlation was significant after adjusting for these factors	Lee et al. (2010)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Psychomotor efficiency, working memory, mental flexibility	WAIS-III digit-symbol test, Trail Making Test	Chronic low back pain	SF-36	No significant correlation observed between cognitive performance and SF-36 pain subscale score	No non-pain comparative group included. No effect of gender, height, weight, depression or opioid medication dose on cognitive performance. Opioid treatment improved cognitive performance over study period	Jamison et al. (2003)
Psychomotor efficiency, working memory, attention, mental flexibility	WAIS-III digit-symbol test, Stroop interference test	Chronic low back pain/lombosciatica, spinal cord injury, osteoarthritis, cervicobrachial neuralgia, postsurgical nerve lesion, multiple sclerosis, CRPS, pachypleuritis n=18	VAS, MPQ	Significant correlation between pain ratings and Stroop interference performance (P= 0.01, r value no quoted)	No non-pain comparative group included. No effect of gender, psychotropic medication use, category of chronic pain or morphine dose on cognitive performance. Morphine treatment improved cognitive performance over study period	Tassain et al. (2003)
Reaction time	Visual reaction time task	Migraine (interictal) n=60	Diagnosis of migraine according to IHS criteria	No correlation analysis performed for cognition and pain ratings	No effect of pain on attention, verbal and visual memory, perceptual-motor coordination, visual perception or abstract reasoning. No effect of anxiety on cognition. Duration of illness and number of migraine attacks per month correlated with cognitive performance	Calandre et al. (2002)
Reaction time and working memory	Verbal and spatial reaction time and working memory tasks	Chronic whiplash-associated disorder n=30	VAS	Significant correlation between verbal reaction time ($r > - 0.80$, $p < 0.05$) and VAS score (rated after task)	Medication discontinued for 16hrs before testing	Antepohl et al. (2003)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Reaction time, psychomotor speed	Continuous reaction time test, finger tapping test	Chronic non-malignant pain n=155	VAS	No correlation analysis performed for cognition and pain ratings	No association between pain and PASAT or MMSE performance. Age, gender, education, sedation and type of medication also influenced cognitive performance	Sjogren et al. (2005)
Reaction time, and visuospatial awareness	Performance assessment battery (Manikin test, psychomotor vigilance and 4CRT test)	Persistent spinal pain n=20	MPQ	Significant correlation between Manikin test accuracy and MPQ pain rating index score (r= -0.301, p = 0.019)	No association between pain anxiety on cognitive performance	Harman and Ruyak (2005)
Perceptual learning ability	2-point discrimination	Complex regional pain syndrome n=12	Medical interview	Significant correlation between two-point discrimination thresholds on affected side and MPQ pain rating index score	Edema and stimulus evoked pain did not affect two-point discrimination theresholds	Maihofner and DeCol (2007)
Executive function	Process dissociation procedure applied to a cued recall task	Chronic musculoskeletal pain and various peripheral neuropathic pain syndromes n=18	NRS	No correlation analysis of task performance and pain rating performed	Medication use did not affect cognition. Pain catastrophising, kinesophobia, pain anxiety symptoms and anxiety scores were negatively correlated with cognitive performance	Grisart and Van der Linden (2001)
Divided and selective attention, verbal learning and memory and spatial memory	Stroop task, PASAT, CVLT, Rey-Osterrieth Complex Figure Test	Chronic whiplash-associated disorder n=31	Quebec task force on Whiplash-associated Disorder classification	No correlation analysis performed for cognition and pain ratings	Whiplash patients had high hypochondriasis and hysteria scores	Bosma and Kessels (2002)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Mental flexibility	D-KEFS Trails Number-Letter Switching test	Chronic lower back pain, osteoarthritis, fibromyalgia, peripheral neuropathy, myofascial pain, osteoporosis, spinal stenosis, headache, gout, vulvodynia, carpal tunnel syndrome, costochondritis, oesophagitis, post-herpetic neuralgia, rheumatoid arthritis, trigeminal neuralgia n=56	SF-MPQ	No significant correlation between D-KEFS Trails Number-Letter Switching and SF-MPQ rating (p=0.056)	Older adult subject cohort. No effect of pain on MMSE score, free or paired recall, or psychomotor speed. No effect of depression, opioid use, sleep disturbances, Cumulative Illness Rating Scale score or education on cognition	Karp et al. (2006)
Executive function and emotional decision making	WCST, IGT	Fibromyalgia n=36	WHYMPI	Significant correlation between WCST (r= -0.23, p=0.03) and IGT (r= -0.25, p=0.02) and pain intensity scores. Significant correlation between WCST (r= -0.25, p=0.02) and IGT (r= - 0.25, p=0.02) and pain interference scores	Female subject cohort. Pain patients showed significantly greater harm avoidance but this did not affect cognition. Years since FM diagnosis and duration of pharmacological treatment were correlated with IGT performance	Verdejo-Garcia et al. (2009)
Emotional decision making	IGT	CRPS, chronic back pain n=38	SF-MPQ	Significant correlation between SF-MPQ rating in chronic back pain group only (r=-0.75, P<0.003)	Pain did not affect WCST performance, attention, short-term memory or general intelligence. Correlation was significant after adjusting for age and pain chronicity	Apkarian et al. (2004a)

Cognitive variable affected	Cognitive tests sensitive to impaired performance	Type of chronic pain	Pain assessment method	Correlation between pain and cognitive performance	Other parameters investigated	Reference
Broad cognitive functioning	MMSE, CCSE	Migraine, cluster headache and chronic daily headache (during headache intervals) n=196	Diagnosis of migraine and cluster headache according to IHS criteria, chronic daily headache met migraine criteria for individual headaches and incidence exceeded 15 days per month	No correlation analysis performed for cognition and pain ratings	No effect of depression on cognition. MMSE and CCSE rating decreased only *during* headache intervals (within subjects design). Gender and age significantly affected cognitive performance	Meyer et al. (2000)
Broad cognitive functioning	MMSE	Diabetic neuropathy, trigeminal neuralgia, CRPS, post-herpetic neuralgia, entrapment syndromes, post-stroke pain, peripheral neuropathies and neuralgias, radiculopathy, lumbar pain, slipped disc, spinal canal stenosis, spondyliosis, spondylothesis, surgical trauma, musculoskeletal pain and rheumatologic causes n=1519	VAS, SF-MPQ	No correlation analysis performed for cognition and pain ratings	Type of pain, age, anxiety, depression and obesity also affected cognition but effect of pain was significant after adjusting for these factors. Gender and time since diagnosis were also accounted for	Povedano et al. (2007)
Broad cognitive functioning	MMSE	FM n=46	SF-MPQ	No correlation analysis performed for cognition and pain ratings	Age, pain severity and presence of anxiety and depression did not affect frequency of cognitive impairment but anxiety and depression scores were higher in FM patients with impaired cognition	Rodriguez-Andreu et al. (2009)

Abbreviations: 4CRT: four choice reaction time test, ACR: American College of Rheumatology, AIMS: Arthritis Impact Measurement Scales, CCSE: Cognitive Capacity Screening Examination, CRPS: Complex Regional Pain Syndrome, CVLT: California Verbal Learning Test, D-KEFS: Delis-Kaplan Executive Function System, IGT: Iowa gambling task, IHS: International Headache society, MPQ: McGill Pain questionnaire, MPI-PS: multidimensional pain inventory pain severity scale, MMSE: Mini Mental State Exam, n: sample size, NRS: numerical rating scale, PPI: present pain intensity, PASAT: Paced Auditory Serial Addition Task, SF-36: Medical Outcomes – short form, RBANS: Repeatable Battery for the Assessment of Neuropsychological Status, SF-MPQ: short-form MPQ, TEA: Test of Everyday Attention, WAIS-R: Weschler Adult Intelligence Scale- Revised, WCST: Wisconsin Card Sorting Test, WHYMPI: West Haven-Yale Multidimensional Pain Inventory, WMS-R: Wechsler Memory Scale – Revised, VAS: visual analogue scale.