

Supplementary Material

Association of Anxiety and Unspecified Emotional Distress Obtained from a Medical Records Linkage System with Incident Cognitive Outcomes in a Population-Based Setting

Supplementary Table 1. Linear Mixed Effects Models

Predictor	N ^a	zMemory		N ^a	zAttention	
		Beta	(95% CI)		Beta	(95% CI)
Anxiety	12,210	-0.144	(-0.230, -0.057)	11,773	-0.137	(-0.221, -0.054)
Time		-0.054	(-0.061, -0.047)		-0.105	(-0.112, -0.098)
Anxiety*Time		-0.017	(-0.029, -0.004)		-0.017	(-0.030, -0.005)
Anxiety w/o Medication	12,203	-0.172	(-0.303, -0.041)	11,766	-0.169	(-0.296, -0.042)
Anxiety w/ Medication		-0.132	(-0.231, -0.034)		-0.119	(-0.215, -0.023)
Time		-0.054	(-0.061, -0.047)		-0.105	(-0.112, -0.098)
Anxiety w/o Medication*Time		-0.014	(-0.034, 0.005)		-0.014	(-0.033, 0.005)
Anxiety w/ Medication*Time		-0.018	(-0.033, -0.003)		-0.019	(-0.033, -0.005)
Anxiety Before Study Only	12,206	-0.181	(-0.275, -0.087)	11,769	-0.135	(-0.226, -0.045)
Anxiety Study Baseline Only		-0.188	(-0.355, -0.021)		-0.386	(-0.550, -0.222)
Anxiety Both		-0.087	(-0.247, 0.073)		-0.321	(-0.476, -0.166)
Time		-0.053	(-0.060, -0.045)		-0.103	(-0.111, -0.096)
Anxiety Before Study Only*Time		-0.018	(-0.032, -0.004)		-0.018	(-0.032, -0.005)
Anxiety Study Baseline Only*Time		-0.017	(-0.043, 0.009)		-0.019	(-0.045, 0.006)
Anxiety Both*Time		-0.019	(-0.043, 0.005)		-0.020	(-0.044, 0.003)
UED	12,187	-0.061	(-0.148, 0.026)	11,751	-0.034	(-0.118, 0.051)
Time		-0.054	(-0.062, -0.047)		-0.106	(-0.113, -0.099)
UED*Time		-0.016	(-0.029, -0.003)		-0.014	(-0.026, -0.001)
UED w/o Medication	12,171	-0.049	(-0.141, 0.043)	11,736	-0.030	(-0.119, 0.059)
UED w/ Medication		-0.151	(-0.343, 0.040)		-0.042	(-0.227, 0.143)
Time		-0.054	(-0.062, -0.047)		-0.106	(-0.113, -0.099)
UED w/o Medication*Time		-0.016	(-0.030, -0.002)		-0.014	(-0.027, -0.001)
UED w/ Medication*Time		-0.013	(-0.041, 0.016)		-0.013	(-0.040, 0.014)

Linear mixed effects models with participant-specific intercepts and slopes for time. All models adjusted for age at baseline, sex, education, *APOE* $\epsilon 4$ allele status, baseline Charlson comorbidity index, and whether this was the first time taking the cognitive test battery. ^aIncludes all longitudinal observations. CI, confidence interval; Time, years since study baseline; w/o, without; w/, with; UED, unspecified emotional distress. The reference level is not having the given neuropsychiatric symptom. Statistically significant results are bolded.

Supplementary Table 2. Linear Mixed Effects Models

Predictor	zLanguage		zVisuospatial	
	N ^a	Beta (95% CI)	N ^a	Beta (95% CI)
Anxiety	11,948	-0.093 (-0.178, -0.007)	11,667	-0.100 (-0.185, -0.015)
Time		-0.074 (-0.081, -0.067)		-0.031 (-0.036, -0.026)
Anxiety*Time		-0.008 (-0.020, 0.004)		-0.007 (-0.017, 0.002)
Anxiety w/o Medication	11,941	-0.121 (-0.251, 0.010)	11,660	-0.034 (-0.164, 0.095)
Anxiety w/ Medication		-0.082 (-0.180, 0.016)		-0.135 (-0.233, -0.038)
Time		-0.074 (-0.081, -0.067)		-0.031 (-0.036, -0.026)
Anxiety w/o Medication*Time		-0.013 (-0.032, 0.006)		-0.017 (-0.031, -0.003)
Anxiety w/ Medication*Time		-0.005 (-0.020, 0.009)		-0.003 (-0.013, 0.008)
Anxiety Before Study Only	11,944	-0.112 (-0.205, -0.018)	11,663	-0.113 (-0.205, -0.020)
Anxiety Study Baseline Only		-0.083 (-0.249, 0.084)		-0.180 (-0.346, -0.013)
Anxiety Both		-0.051 (-0.210, 0.107)		-0.130 (-0.289, 0.029)
Time		-0.074 (-0.082, -0.067)		-0.031 (-0.036, -0.025)
Anxiety Before Study Only*Time		-0.002 (-0.015, 0.012)		-0.009 (-0.019, 0.001)
Anxiety Study Baseline Only*Time		0.001 (-0.024, 0.027)		-0.001 (-0.020, 0.018)
Anxiety Both*Time		-0.030 (-0.053, -0.007)		-0.003 (-0.021, 0.014)
UED	11,922	0.009 (-0.077, 0.095)	11,645	-0.025 (-0.111, 0.061)
Time		-0.073 (-0.080, -0.066)		-0.032 (-0.037, -0.027)
UED*Time		-0.013 (-0.025, 0.000)		-0.003 (-0.012, 0.006)
UED w/o Medication	11,906	0.003 (-0.088, 0.094)	11,629	-0.025 (-0.115, 0.066)
UED w/ Medication		0.043 (-0.148, 0.233)		-0.010 (-0.198, 0.178)
Time		-0.073 (-0.080, -0.066)		-0.032 (-0.037, -0.027)
UED w/o Medication*Time		-0.013 (-0.026, 0.001)		-0.002 (-0.012, 0.008)
UED w/ Medication*Time		-0.013 (-0.040, 0.015)		-0.009 (-0.029, 0.011)

Linear mixed effects models with participant-specific intercepts and slopes for time. All models adjusted for age at baseline, sex, education, *APOE* ε4 allele status, baseline Charlson comorbidity index, and whether this was the first time taking the cognitive test battery. ^aIncludes all longitudinal observations. CI, confidence interval; Time, years since study baseline; w/o, without; w/, with; UED, unspecified emotional distress. The reference level is not having the given neuropsychiatric symptom. Statistically significant results are bolded.

Supplementary Table 3. Medications Considered in Medical Records Abstraction

Generic	Brand
Selective Serotonin Reuptake Inhibitors (SSRI)	
citalopram hydrobromide	Celexa
escitalopram oxalate	Lexapro
fluoxetine	Sarafem
fluoxetine hydrochloride	Prozac
fluvoxamine Maleate	Luvox
paroxetine mesylate	Pexeva
paroxetine Hydrochloride	Paxil
sertraline Hydrochloride	Zoloft
other	
Tricyclics	
Amitriptyline	Elavil or Vanatrip
Clomipramine	Anafranil
Doxepin Hydrochloride	Sinequan
Imipramine Hydrochloride	Tofranil
Imipramine Pamoate	Tofranil-PM
Trimipramine	Surmontil
Desipramine Hydrochloride	Norpramin
Nortriptyline Hydrochloride	Pamelor, Aventyl
maprotiline	Ludiomil
Protriptyline Hydrochloride	Vivactil
other	
Monoamine Oxidase Inhibitors (MAOI)	
Isocarboxazid	Marplan
Phenelzine	Nardil or Nardelzine
	l-deprenyl, Eldepryl, Selapar, Anipryl,
Selegiline	Emsam
Tranylcypromine Sulfate	Parnate
other	
Noradrenergic and 5-HT	
Mirtazapine	Remeron
other	
Norepinephrine - Dopamine Reuptake Inhibitor (DNRI)	
Bupropion	Wellbutrin, Zyban
other	
Serotonin - Norepinephrine Reuptake Inhibitor (SNRI)	
Desvenlafaxine	Pristiq
Duloxetine	Cymbalta or Yentreve
Venlafaxine Hydrochloride	Effexor
other	

Other Antidepressants

Nefazodone Hydrochloride	Serzone
Trazodone Hydrochloride	Desyrel
Amoxapine	Asendin
vilazodone	
other	

Combination Antipsychotic and Antidepressant Medication

Olanzapine; fluoxetine hydrochloride	Symbyax (Combination Antipsychotic and Antidepressant Medication)
other	

Anti-Psychotics

Clozapine	Clozaril
Olanzapine	Zyprexa
Quetiapine Fumarate	Seroquel
Risperidone	Risperdal
Ziprasidone Hydrochloride	Ziprasidone
Aripiprazole	Abilify
Chlorpromazine Hydrochloride	Thorazine
Fluphenazine Hydrochloride	Prolixin
Haloperidol Decanoate	Haldol
iloperidone	Fanapt
Perphenazine (generic only)	
pimozide (for Tourette's syndrome)	Orap
Prochlorperazine	Compazine
Thioridazine Hydrochloride	Mellaril, (generic too)
Trifluoperazine Hydrochloride	Stelazine
Loxapine Succinate	Loxapac, Loxitane
molindone	Moban
paliperidone	Invega
Thiothixene	Navane
other	

Other Anxiolytics

Buspirone Hydrochloride	BuSpar
Hydroxyzine	Atarax, Vistaril
Meprobamate	Equanil
other	

Benzodiazepines

Midazolam Hydrochloride	Versed
Temazepam	Restoril
Triazolam	Halcion
Alprazolam	Xanax
Chlordiazepoxide Hydrochloride	Librium

Clonazepam	Klonopin
Clorazepate Dipotassium	Tranxene
Diazepam	Valium
Lorazepam	Ativan
oxazepam (generic only)	
other	

Sedatives/hypnotics

Chloral Hydrate	Noctec
Phenobarbital	Luminal
Thiopental Sodium	Thiopental
Zolpidem Tartrate	Ambian
other	

(NERI)

O-Desmethyl venlafaxine
other

Mood Stabilizing and Anticonvulsant Medication

carbamazepine	Tegretol
divalproex sodium (valproic acid)	Depakote
gabapentin	Neurontin
lamotrigine	Lamictal
lithium carbonate	Eskalith, Lithobid
lithium citrate (generic only)	
oxcarbazepine	Trileptal
topiramate	Topamax
other anti-Epileptic Drug, specify	

Other (not included above)
