GENDER DIFFERENCES IN NEUROPSYCHIATRIC SYMPTOMS ARE ATTENUATED BY EDUCATION AND COGNITIVE ABILITY

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ABSTRACT

BACKGROUND: One of the more consistent findings in gender medicine is the difference in symptom self-report: women are more prone to report physical symptoms than men are. In patients with neuropsychiatric disorders, gender differences in symptom-report are reported less consistently.

METHOD: A retrospective, cross-sectional study of patients who were evaluated with the Neuropsych Questionnaire, an internet-based symptom rating system, and CNT, a computerized neurocognitive test battery.

SUBJECTS: 1823 patients, age 18 to 65, with diverse neuropsychiatric disorders, evaluated at one of the Neuropsychiatry Clinics in Chapel Hill, Charlotte or Raleigh, NC.

RESULTS: Gender differences in symptom self-report showed a consistent pattern in patients and female patients rate their symptoms about 10% higher than male patients. The female preponderance is most strongly seen in measures of anxiety, depression and somatic symptoms. A male preponderance is noted in measures of mania, aggression, learning problems and substance abuse. The effect sizes attributable to gender are very small, however, and are dwarfed by group differences in education and cognition.

CONCLUSIONS: Higher levels of education and cognitive ability are associated with lower symptom self-report. and attenuate the gender effect. Studies of gender differences should apply the appropriate controls for these variables.

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GENDER DIFFERENCES IN NEUROPSYCHIATRIC DISORDERS ARE ATTENUATED BY EDUCATION AND COGNITIVE ABILITY

One of the more consistent findings in gender medicine is the difference in symptom self-report: women are more prone to report physical symptoms than men are. There are, of course, gender differences in morbidity. At every age except early childhood, women are more frequently ill than men, albeit with comparatively mild problems; men feel ill less often, but their illnesses and injuries tend to be more serious.(Verbrugge, 1982) However, gender differences in symptom report cannot be imputed just to morbidity differences. Even in healthy people, health surveys, studies of physical symptom self-report and medical registration of physical complaints find consistent gender differences in symptom reporting. The female excess of symptom self-report is independent of the symptom measure, response format and time frame used, and the population under study.(Van Roy, Grøholt, Heyerdahl, & Clench-Aas, 2006)(Iburg, Rasmussen, & Avlund, 2006)(van Wijk & Kolk, 1997)(Ladwig, Marten-Mittag, Formanek, & Dammann, 2000)(Kroenke & Spitzer, 1998)

With respect to neuropsychiatric disorders, studies of symptom self-report are less consistent. In depression, for example, studies have reported no significant gender differences (Bogner & Gallo, 2004), higher rates of symptom self-report in women (Kornstein et al., 2000)(van Noorden et al., 2010) or differences in the symptom profiles of depressed men and women.(Dekker, Koelen, Peen, Schoevers, & Gijsbers-van Wijk, 2007) Alternatively, women report more symptoms (Kockler & Heun, 2002) but there are “no great differences” in observer rating scales.(Poutanen, Koivisto, Mattila, Joukamaa, & Salokangas, 2009)

In another common disorder, ADHD, some have found that males and females are more similar than different, and that symptom profiles are not sex specific.(Rucklidge, 2010)(Biederman & Faraone, 2004)(DuPaul et al., 2001)(Schaughency, McGee, Raja, Feehan, & Silva, 1994) Others have reported higher symptom rates in males (Dong Hun Lee, Oakland, Jackson, & Glutting, 2008)(Newcorn et al., 2001) or higher rates in women.(Robison et al., 2008) Girls with ADHD are either more likely (Quinn, 2008) or less likely (Biederman et al., 2002) to be diagnosed with comorbid depression.

In studies of concussion, reports have indicated that female athletes endorse more baseline symptoms than male athletes.(Covassin et al., 2006) Women report more enduring symptoms following concussion, including depression, perceived chronic stress, pain, memory difficulties, and somatic symptoms.(Bay, Sikorskii, & Saint-Arnault, 2009)(Dick, 2009)(Bazarian, Blyth, Mookerjee, He, & McDermott, 2010) Alternatively, they may be at increased risk for post-traumatic headache but not other post-traumatic symptoms.(Jensen & Thulstrup, 2001)

The divergence of research findings is probably explicable in terms of small numbers, reliance on rating instruments that measure only a narrow spectrum of symptoms, and, in clinical populations, referral bias. In this study, we could not escape the latter complication, but we were able address the first two, presenting data from a large group of patients with diverse neuropsychiatric disorders, evaluated with a broad-spectrum symptom questionnaire, and in search of a more coherent interpretation of gender differences in symptom self-report.

METHOD

This was a retrospective, cross-sectional study of 1823 patients, age 18 to 65, evaluated at the Neuropsychiatry Clinics in Chapel Hill, Charlotte and Raleigh over a three-year period. As part of a comprehensive neuropsychiatric evaluation, patients were administered a 201 item symptom questionnaire and a battery of neurocognitive tests. Patients gave written informed consent to the use of their de-identified clinical data for the purposes of research and program evaluation.

NP3: THE NEUROPSYCH QUESTIONNAIRE

The Neuropsych Questionnaire (NP3) is a computerized symptom checklist that is comprised of 201 items, or questions, whether a symptom is present, or if so, if it is mild, moderate or severe. Items are grouped into twenty symptom scales, derived by factor analysis. The symptom scales refer to general symptom categories, e.g., depression, anxiety, inattention, etc. The symptom scales, in turn, fall into four factors: anxiety-depression, cognition, mania and somatic. (See supplemental materials). Each item is scored as 0-1-2-3. The items in each symptom scale are averaged, and then multiplied by 100; so, a patient's symptom scale score, for depression, for example, can range from a low of zero to a high of 300. The NP3 generates no fewer than 25 scores: the 20 symptom scale scores, the four factor scores and the average symptom score, the average of the 20 scale scores.

The CNT Battery

The CNT used in this study, an updated version of the CNS Vital Signs test battery, is a screening measure of cognitive functioning that contains seven tests and generates eight test scores. The CNS Vital Signs test battery has been widely used by neurologists, psychiatrists and neuropsychologists. (Gualtieri & Johnson, 2006) Seven of the 8 test scores in the CNT load on three factors, memory, attention and information processing speed. The tests generate raw scores and standard scores. Scores are standardized by adjusting for age and education, based on data from 3,420 normal participants (age 4 to 90). The CNT battery generates both raw scores and standard scores. Standard scores are reported with a mean of 100 with a standard deviation of 15. A single summary score, the Index score (INDEX), is computed by averaging the standard scores of the three factor scores (Table 2). Factor scores and the Index are derived from standard scores.

TABLE 1. THE CNT

TEST	ABBREV	FACTOR	SCORE
Verbal Memory Test	VBM	MEM	Correct responses minus errors
Visual Memory Test	VIM	MEM	Correct responses minus errors
Finger Tapping Test	FTT	*	Total number of taps, right and left
Symbol Digit Coding Test	SDC	PS	Correct responses minus errors in two minutes
Stroop Test	RT	PS	Average of complex and Stroop response times
	ST	ATT	Number of errors in non-congruent condition
Shifting Attention Test	SAT	PS	Correct responses minus errors
Continuous Performance Test	CPT	ATT	Correct responses minus errors

*The finger tapping test does not load onto to any of the three factors.

Test-retest reliability and the concurrent validity of CNT are comparable to similar, conventional neuropsychological tests.(Gualtieri & Johnson, 2006) Research has indicated relevance to the study of mood disorders (Iverson, Brooks, Langenecker, & Young, 2011), sleep disorders (Armstrong, L., Glidewell, R., Orr, W., & Roby, E., 2011), encephalopathy (Brooks & Barlow, 2011) post-concussion syndrome and severe traumatic brain injury (Gualtieri & Johnson, 2008).

SUBJECTS

In the NCNC database, there were 1863 patients who were age 18-65 and had completed the NP3 and CNT on the same day as part of an initial evaluation. Diagnoses were based on a comprehensive examination, of which NP3 and CNT were only a part. The patients were classified into four groups according to their primary diagnosis. Psychiatric diagnoses were made on the basis of DSM-IV TR criteria, where applicable, and affirmed by review by a research psychiatrist (CTG). Cognitive disorders (N = 452) included ADHD, learning disability and

cognitive disorder NOS. Patients with medical conditions (N = 107) had chronic pain or fatigue associated with fibromyalgia, hypothyroidism or cancer. The neurological diagnoses (N = 355) are listed in Table 1. The three most frequent diagnoses were attention deficit hyperactivity disorder (ADHD), major depression (DEP) and traumatic brain injury (TBI).

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS

DIAGNOSIS	ALL	M	F	AGE	EDUC	COMFAM	%WHITE
PSYCHIATRIC DISORDERS	**949**	**382**	**567**	**37.09**	**14.13**	**2.69**	**0.77**
Major Depression	327	108	219	39.2	14.4	2.71	0.78
Bipolar Disorder	146	36	110	38.3	14.1	2.73	0.76
Generalized Anxiety	138	52	86	36.3	14.5	2.75	0.83
Post-Traumatic Stress Disorder	72	24	48	39.7	13.7	2.61	0.69
Mood Disorder	67	30	37	34.3	13.6	2.42	0.85
Obsessive-Compulsive Disorder	51	34	17	32.5	15.1	2.88	0.80
Substance Abuse	43	37	6	24.8	12.7	2.85	0.60
Conversion Disorder	35	18	17	44.1	12.5	2.27	0.77
Autism Spectrum	19	14	5	32.1	13.3	2.63	0.74
Schizophrenia	17	7	10	35.5	14.3	2.38	0.59
Social Anxiety	11	9	2	36.3	15.7	2.89	0.91
Alcohol	10	9	1	33.5	14.9	2.80	0.70
Tourettes	6	4	2	20.5	12.0	2.67	1.00
Borderline Personality	5		5	40.6	14.0	3.00	0.40
Eating Disorder	2		2	33.5	14.0	3.00	0.50
NEUROLOGICAL CONDITIONS	**355**	**223**	**132**	**43.64**	**13.98**	**2.46**	**0.81**
Traumatic Brain Injury	215	154	61	43.1	13.5	2.38	0.80
Mild Cognitive Impairment	33	8	25	52.3	14.7	2.70	0.88
Post Concussion Syndrome	21	18	3	41.5	13.9	2.43	0.71
Stroke	18	7	11	48.6	15.8	2.71	0.94
Epilepsy, Seizures	18	5	13	32.4	13.9	2.67	0.67
Dementia	8	5	3	43.6	12.5	2.00	0.75
Parkinsons, Huntingtons	8	6	2	51.0	15.6	2.80	1.00
Multiple Sclerosis	7	1	6	48.3	16.7	2.71	1.00
Encephalitis	6	1	5	38.0	15.3	2.20	1.00
Headache	6	6		38.7	14.6	2.20	0.67
Electrocution	6	5	1	34.2	13.6	2.67	0.50
Mild Brain Injury	3	3		41.3		1.00	1.00
Anoxic Brain Injury, Carbon Monoxide	3	1	2	46.0	16.7	3.00	1.00
Brain Tumor	3	3		46.0		3.00	1.00
COGNITIVE DISORDERS	**452**	**226**	**226**	**43.64**	**13.98**	**2.46**	**0.81**
Attention Deficit Hyperactivity Disorder	432	219	213	30.1	14.6	2.84	0.80
Cognitive Disorder NOS	13	4	9	45.9	14.5	2.69	0.92
Learning Disability	5	3	2	22.8	12.6	2.40	0.80
Subjective Experience Of Cognitive Impairment	2		2	48.5	15.0	2.50	1.00
MEDICAL CONDITIONS	**107**	**50**	**57**	**44.79**	**13.29**	**2.29**	**0.76**
Chronic Pain	90	49	41	45.8	13.1	2.19	0.73
Fibromyalgia	12		12	39.9	14.4	2.92	0.83
Fatigue, Chronic Fatigue	2	1	1	42.5	15.5	3.00	1.00
Cancer	2		2	42.0	14.0	3.00	1.00
Thyroid	1		1	31.0	12.0	2.00	1.00
ALL DIAGNOSES	**1863**	**881**	**982**	**37.20**	**14.16**	**2.66**	**0.79**

ANALYSIS

Data were normalized, when necessary, by log transformation or standardization to a mean of 100 and standard deviation of 15. Outliers were defined as 6 SD's above or below the mean. Outliers were not more likely to occur in one gender or another, but were more frequent in the low education/cognition group. Thus, eliminating outliers therefore worked *against* the hypothesis that education/cognition had a significant effect. Correlations were by Pearson product-moment correlation. Analysis of differences was by MANOVA with covariates as specified. Effect sizes were calculated by Cohen's d or partial *eta* squared as specified.

RESULTS

The overall expression of symptoms, as expressed by the average symptom score (AVGSxS) was associated with age, race, education level and cognitive ability (the Index score).(Table 3) Correlation analysis for the total group, for males and for females, indicated that symptom expression in all of the scales (except substance abuse) was lower in patients with more education and higher cognitive ability (negative correlations significant at the level of $P < 0.01$). Older patients reported more symptoms (positive correlations at the $P < 0.01$ level) in the memory and learning scales and the agoraphobia, depression, pain, fatigue, sleep and somatic scales. Correlations with race were hardly ever significant or meaningful.

TABLE 3. CORRELATIONS OF AVERAGE SYMPTOM SCORE

All Ss	AVGSxS	AGE	EDUC	RACE	COMPNUM	INDEX
AVGSxS	1	.032**	-.297**	.076**	-.228**	-.350**
AGE	.032**	1	.076**	.005	-.285**	-.184**
EDUC	-.297**	.076**	1	-.147**	.442**	.342**
RACE	.076**	.005	-.147**	1	-.107**	-.184**
COMFAM	-.228**	-.285**	.442**	-.107**	1	.380**
INDEX	-.350**	-.184**	.342**	-.184**	.380**	1
Males						
AVGSxS	1	.068**	-.320**	.070**	-.237**	-.337**
AGE	.068**	1	-.037**	-.024**	-.374**	-.217**
EDUC	-.320**	-.037**	1	-.211**	.526**	.354**
RACE	.070**	-.024**	-.211**	1	-.124**	-.204**
COMFAM	-.237**	-.374**	.526**	-.124**	1	.392**
INDEX	-.337**	-.217**	.354**	-.204**	.392**	1
Females						
AVGSxS	1	-.002	-.288**	.078**	-.236**	-.369**
AGE	-.002	1	.180**	.027**	-.200**	-.156**
EDUC	-.288**	.180**	1	-.110**	.328**	.322**
RACE	.078**	.027**	-.110**	1	-.109**	-.177**
COMFAM	-.236**	-.200**	.328**	-.109**	1	.358**
INDEX	-.369**	-.156**	.322**	-.177**	.358**	1

Gender differences in the cognitive scores on CNT were statistically significant at the $P < 0.0001$ level(MANOVA, controlling for age, race, education and computer familiarity). The effect sizes were not very large, however; the highest was 0.15 (Cohen's d). Women scored higher in verbal memory ($d = 0.28$) and men scored higher in finger tapping ($d = 0.21$). (Table 4)

TABLE 4. COGNITIVE PERFORMANCE IN MALES AND FEMALES

	M	F	d	F	Sig.
VBM	47.89	49.91	-0.28	38.173	.000
VIM	43.41	43.65	-0.04	33.032	.000
SDC	44.74	47.56	-0.16	95.715	.000
RT	698.25	685.79	0.07	19.747	.000
SAT	34.22	34.72	-0.02	66.963	.000
ST	29.40	26.70	0.09	6.569	.000
CPT	28.41	32.70	-0.15	2.456	.032
FTT	103.72	96.66	0.21	52.809	.000

When gender differences in symptom self-report were examined, age, race, education, computer familiarity and the Index score of the CNT were included as covariates. MANOVA for the entire patient group indicated significant differences in all of the NP3 parameters: the twenty symptom scales, the four symptom factors, and the average symptom score. Overall, female subjects rated their symptoms 10% higher than males; but, again, the effect sizes were not very big. The average symptom score for 881 male patients was 82.3 and for 983 female patients, 90.8 ($F = 39.1$, $P < 0.0001$). In Table 5, females scored significantly higher in all of the symptom scales of those the anxiety-depression and somatic. The only effect sizes that were even "small" occurred in the somatic and anxiety-depression scales. Males rated themselves higher in learning problems, mania, aggression and substance abuse but nothing else.

TABLE 5. NP3 SCORES, ALL SUBJECTS, BY GENDER

	MALE	SD	FEMALE	SD	d	F	Sig.
AVERAGE SYMPTOM SCORE	82.34	49.68	90.76	48.62	-0.17	39.048	.000
COGNITIVE FACTOR (CF)	117.59	69.75	123.97	70.34	-0.09	56.344	.000
MANIA FACTOR (MF)	71.39	51.84	71.62	49.76	0.00	29.890	.000
SOMATIC FACTOR (SF)	83.45	66.52	101.41	66.17	-0.27	19.202	.000
ANXIETY DEPRESSION FACTOR (ADF)	79.01	57.53	93.40	59.85	-0.24	34.029	.000
FATIGUE (FTG)	124.1	91.2	152.9	90.2	-0.31	18.581	.000
PANIC	57.2	70.6	79.2	80.4	-0.29	18.719	.000
DEPRESSION (DEP)	108.7	76.0	129.7	80.5	-0.26	6.281	.000
ANXIETY (ANX)	120.8	78.3	138.7	77.7	-0.23	31.696	.000
SOMATIC (SOMA)	48.6	54.1	61.2	58.2	-0.22	11.148	.000
AGORAPHOBIA (AGORA)	56.6	62.9	67.7	69.4	-0.17	64.708	.000
PAIN	77.6	77.7	90.2	78.7	-0.16	21.130	.000
MEMORY (MEM)	100.0	71.2	110.6	72.3	-0.15	31.782	.000
ATTENTION (ATT)	142.2	82.5	152.8	83.0	-0.13	28.185	.000
PSYCHOSIS (PSYCH)	56.2	55.0	63.2	58.8	-0.12	19.881	.000
SLEEP	126.5	100.6	138.7	101.9	-0.12	34.198	.000
SOCIAL ANXIETY (SAD)	76.0	70.8	84.6	72.5	-0.12	33.197	.000
OBSESSIONS & COMPULSIONS (OC)	54.7	50.6	60.5	48.5	-0.12	15.846	.000
MOOD STABILITY (MS)	102.5	75.1	110.9	76.0	-0.11	27.898	.000
SUICIDE (SUI)	52.9	73.6	59.1	79.5	-0.08	25.443	.000
HYPERACTIVE-IMPULSIVE (HIP)	98.0	68.7	98.8	66.2	-0.01	14.750	.000
LEARNING PROBLEMS (LPX)	110.6	71.1	108.5	69.9	0.03	42.255	.000
MANIA	50.9	51.1	45.5	49.2	0.11	31.387	.000
AGGRESSION (AGG)	49.3	59.7	39.6	49.5	0.18	25.126	.000
SUBSTANCE ABUSE (SA)	32.6	58.3	22.5	44.0	0.20	4.452	.000

NOTE Table 2. Symptom scales of the anxiety-depression factor are highlighted in yellow. Symptom scales of the somatic factor are highlighted in orange.

A secondary analysis was done, examining the three neuropsychiatric categories: patients with psychiatric, neurological and cognitive disorders; and then, examining the largest single diagnostic group in each category, depression, ADHD and TBI. Table 3 presents the relative strengths of gender differences in all the subjects (expressed as $score_{FEMALE}/score_{MALE}$), and separately in patients in the three major categories, and then in patients with depression, ADHD and TBI. The M/F differences are more or less consistent across the categories. The only anxiety-depression or somatic scales that are expressed more strongly in males than females is the obsessive-compulsive scale in patients with neurological disorders and the somatic and pain scales in TBI patients. Mania and aggression symptoms are always expressed more strongly by males.

TABLE 6. GENDER DIFFERENCES IN ALL PATIENTS AND BY DIAGNOSTIC CATEGORY

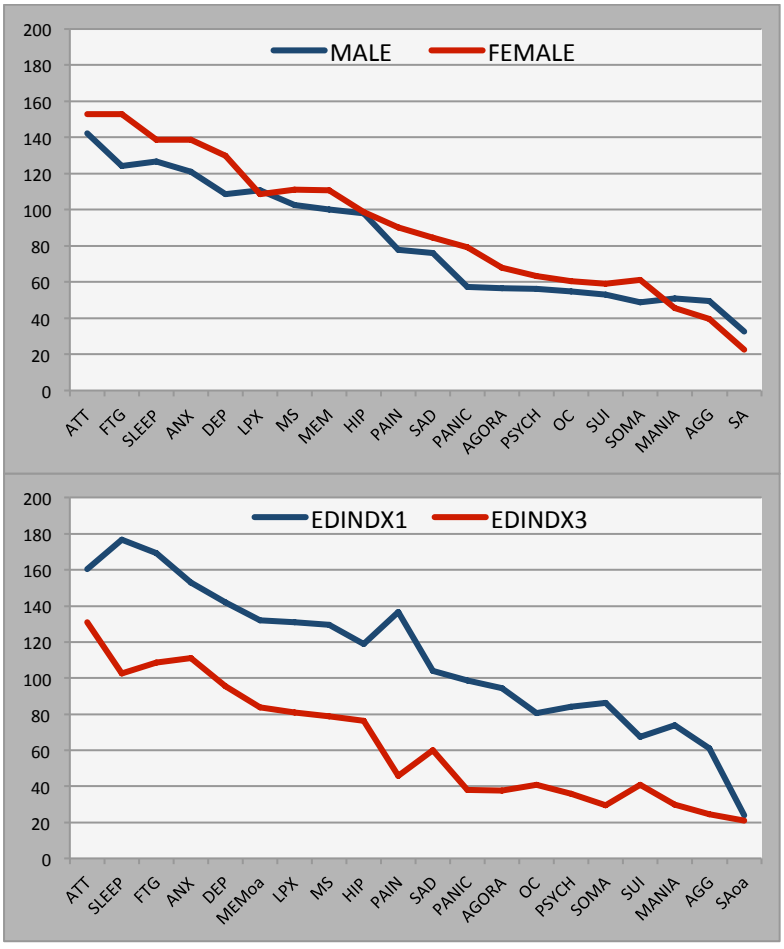
ALL		PSYCH		NEURO		COG		DEP		ADD		TBI	
PANIC	**1.37**	**SOMA**	**1.3**	**SUI**	**1.26**	**PANIC**	**1.91**	**PAIN**	**1.30**	**PANIC**	**1.68**	*SA*	*1.49*
SOMA	**1.25**	**PANIC**	**1.24**	**FTG**	**1.25**	**SOMA**	**1.57**	**SOMA**	**1.25**	*PAIN*	*1.28*	**ATT**	**1.29**
FTG	**1.23**	**PAIN**	**1.22**	**ATT**	**1.24**	**PAIN**	**1.43**	**PANIC**	**1.24**	**SOMA**	**1.25**	**FTG**	**1.29**
DEP	**1.19**	**FTG**	**1.22**	**PANIC**	**1.22**	*AGORA*	*1.29*	**FTG**	**1.19**	*FTG*	*1.19*	**LPX**	**1.20**
AGORA	**1.18**	**DEP**	**1.16**	**AGORA**	**1.2**	**FTG**	**1.29**	**AGORA**	**1.17**	*MS*	*1.16*	**MEM**	**1.20**
PAIN	**1.17**	**MEM**	**1.15**	**MEM**	**1.15**	*SAD*	*1.22*	**PSYCH**	**1.17**	**ANX**	**1.16**	**AGORA**	**1.17**
ANX	**1.16**	**AGORA**	**1.14**	**ANX**	**1.13**	**OC**	**1.2**	*DEP*	*1.12*	**DEP**	**1.14**	**ANX**	**1.12**
OC	**1.14**	**ANX**	**1.12**	**DEP**	**1.12**	**ANX**	**1.19**	**MEM**	**1.12**	**OC**	**1.13**	**PANIC**	**1.12**
SAD	**1.11**	**SLEEP**	**1.11**	*SA*	*1.11*	**PSYCH**	**1.19**	**MS**	**1.10**	**PSYCH**	**1.10**	*DEP*	*1.10*
PSYCH	**1.11**	**OC**	**1.09**	**SLEEP**	**1.11**	**DEP**	**1.18**	**SLEEP**	**1.10**	**MEM**	**1.09**	*SUI*	*1.09*
SLEEP	**1.1**	**PSYCH**	**1.08**	**SAD**	**1.1**	MS	1.15	**ATT**	**1.08**	*SAD*	*1.09*	**SAD**	**1.04**
MEM	**1.1**	**ATT**	**1.08**	**SOMA**	**1.07**	**MEM**	**1.12**	**ANX**	**1.05**	**AGORA**	**1.08**	**HIP**	**1.02**
ATT	**1.09**	**MS**	**1.06**	**LPX**	**1.06**	*HIP*	*1.07*	**OC**	**1.05**	*HIP*	*1.08*	**SLEEP**	**1.00**
MS	**1.07**	*SUI*	*1.05*	**PAIN**	**1.02**	*SLEEP*	*1.07*	**LPX**	**1.04**	*ATT*	*1.03*		
SUI	**1.07**	**SAD**	**1.04**			**ATT**	**1.03**	**SAD**	**1.04**			**MANIA**	**0.99**
HIP	**1.02**			**HIP**	**1**					**LPX**	**0.97**	**SOMA**	**0.98**
		LPX	**1**	**PSYCH**	**0.99**	**LPX**	**0.99**	***SUI***	***1.00***	*SLEEP*	*0.96*	*OC*	*0.98*
LPX	**1**	**HIP**	**0.98**	**OC**	**0.98**	**SUI**	**0.95**	**HIP**	**0.96**	**SUI**	**0.93**	**PAIN**	**0.96**
MANIA	**0.89**	**MANIA**	**0.85**	**MS**	**0.89**	**MANIA**	**0.84**	**AGG**	**0.95**	**AGG**	**0.79**	**MS**	**0.90**
AGG	**0.79**	**AGG**	**0.78**	**MANIA**	**0.87**	**AGG**	**0.74**	**MANIA**	**0.89**	**MANIA**	**0.77**	**PSYCH**	**0.84**
SA	**0.68**	**SA**	**0.64**	**AGG**	**0.72**	**SA**	**0.51**	*SA*	*0.56*	*SA*	*0.58*	**AGG**	**0.62**

NOTE, Table 3. Scales in the anxiety-depression and somatic factors are highlighted as in Table 2. Scale scores that are significantly different at the $P < 0.01$ level are in bold. Scales that do not show gender differences are in italic.

Although gender differences are statistically significant and show a consistent female preponderance in somatic and anxiety-depression symptoms, the effect sizes are small, ranging from 0.0 to 0.31 (average d, 0.10). In order to place these gender differences in the proper perspective, they should be compared to the effects of education and cognition of symptom expression. To this end, we selected a stratified subgroup of 237 men and women who were in the lowest third by education and cognition and 246 who were in the highest third. The two groups were compared by MANOVA, controlling for age and race. Significant differences – higher symptom scores in the lower group – were expressed in 24 out of 25 variables generated by the NP3. In contrast to gender differences, the effect sizes of symptom scale scores resulting from social and intellectual differences ranged from 0.35 to 1.74, average d = 0.94). The average symptom score of the low education/cognition group was 111.2 and for the high group, 63.7 ($F = 40.45$, $P < 0.0001$). (See supplemental materials, Table 3.)

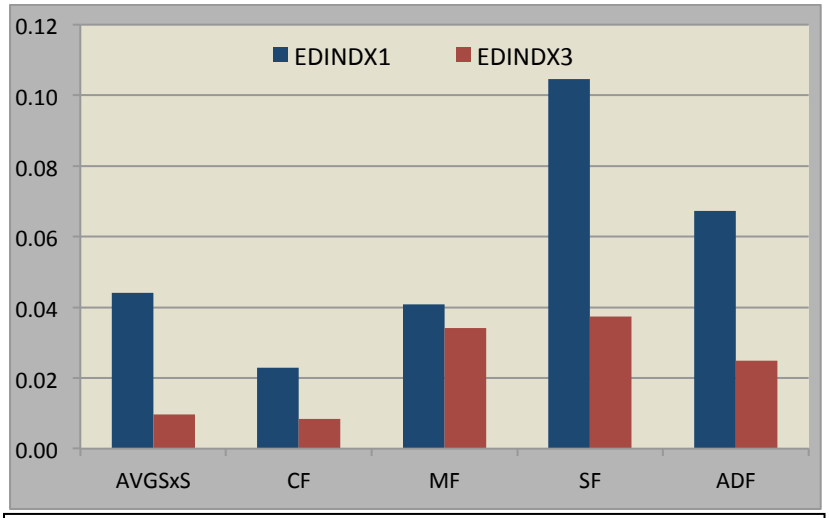
Figures 1a and 1b present the data graphically. The average scores from each of the 20 symptom scales are plotted in Figure 1a for males and females and in Figure 1b for high and low education-cognition groups. Gender differences are decidedly smaller.

FIGURES 1A AND 1B. GENDER DIFFERENCES IN 20 SYMPTOM SCALE SCORES AND DIFFERENCES BY HIGH AND LOW EDUCATION/COGNITION



The final analysis examined the relationship between education/cognition and gender differences. In the lowest group there were 138 men and 99 women and in the highest group, 113 men 133 women. In each group, MANOVA generated significant differences by gender for most of the NP3 parameters. The size of the effect was measured by partial *eta* squared, an alternative statistic for measuring effect size, and representing the variance in NP3 scores explained by gender, controlling for race and age. In Figure 2, *eta* (the y axis) is higher for the average symptom score and for the four factor scores. Education and cognitive ability together, therefore, attenuate the effect size of gender.

FIGURE 2. GENDER DIFFERENCES IN LOW AND HIGH EDUCATION/COGNITION GROUPS



Note, Figure 2. The y axis is partial *eta* squared, an effect size measure that captures the variance in symptom scores attributable to gender differences.

DISCUSSION

It is well-established in medicine in general (Grady et al., 2009)(Heitger, Jones, Frampton, Ardagh, & Anderson, 2007)(Zeltzer et al., 2008) and psychiatry in particular (Steer & Henry, 1979)(Trivedi et al., 2006)(Hanel et al., 2009) that education and intelligence are related to patients' symptom expression and to other, more direct measures of morbidity. Gender differences in symptom self-report are also consistently noted, albeit with exceptions as noted earlier. In this report we note the same patterns in a clinical population of patients with diverse neuropsychiatric disorders. As a general rule, female patients rate their symptoms about 9% higher than male patients. The effect sizes of the gender differences are very small, however, and are dwarfed by group differences in education/cognition. Higher levels of education and cognitive ability are associated with lower symptom self-report. More interesting, higher education and cognitive ability attenuate the gender effect.

In the broad patient categories and in the three largest diagnostic groups, women are consistently prone to report more somatic, anxiety and depression symptoms. However, men tend to report more symptoms of mania and aggression (which may be why women are anxious and depressed). Men often report more learning problems and substance abuse. Diagnostic category has little effect on this pattern: whether the patient has a psychiatric or a neurological or a cognitive disorder, or depression, ADHD or brain injury.

The sample we studied is vulnerable to the same referral bias that has compromised other such clinical studies. The inclusion of patients with a wide range of different diagnoses is also a potential problem, especially

since the relative numbers of patients with different diagnoses is not necessarily reflective of the prevalence of the disorders. Most of the disorders have different prevalence rates in men and women and many are characterized by different symptom patterns in the genders. These facts represent important weaknesses. One's willingness to accept our findings as generally relevant must be tempered by these considerations. However, one also must acknowledge the large number of patients in this survey, the use of a broad-based symptom questionnaire and the fact that our findings are in accord with studies of normal people and patients with a wide range of medical conditions. Also, when the patients are divided into three general categories, and when the three largest diagnostic groups in each category are evaluated separately, the same patterns occur: women more frequently complain of somatic and anxiety-depression symptoms, men more mania and aggression.

The study of a large, diverse, sample is an advantage in that it allows a pattern to emerge that may be thought to transcend diagnosis – even something as fundamental to one's subjective experience as a neuropsychiatric disorder. If anything, our result is reflective of the studies of personality in normal populations. Studies of gender differences in personality have consistently found that men tend to be more assertive and women report themselves to be higher in "neuroticism." (Feingold, 1994)(Costa, Terracciano, & McCrae, 2001)(Schmitt, Realo, Voracek, & Allik, 2008)

However, studies of personality differences have also been consistent in demonstrating that gender differences are small relative to individual variation within genders.(Costa et al., 2001) This fact speaks to the more important point of the report. It is worthwhile to correct the occasional report that the genders do not differ in self-report of neuropsychiatric symptoms, but the more important contribution of this study is to put gender differences in perspective. Gender differences are statistically significant but the effect sizes they generate are very small. They are much smaller than the differences in symptom report that occur relative to education and cognition. Nine points separate the average symptom scores of men and women; 47 points separate the high and low education/cognition groups – an effect size of 0.17 compared to 1.27.

In any clinical sample, it is possible that the female patients report more symptoms because they have more severe conditions or more comorbidity. In fact, one hypothesis to explain gender differences in symptom self-report is based on the assumption that women experience more morbidities than men.(Green & Pope, 1999) It is a weakness of our study that we do not have an independent measure of the severity of the patient's disorder. We do have one indirect measure, however, in the patients' performance on a battery of neurocognitive tests, and female patients performed better than men in most measures. That doesn't prove that the female patients were less severe, but it does suggest that their disorders were not more severe.

Not surprisingly, there are numerous theories, evolutionary, neuro-endocrine, psychological and sociological, to explain gender differences in morbidity and symptom expression.(van Wijk & Kolk, 1997) That educational level reduces the magnitude of gender differences has been reported before (Van de Velde, Bracke, & Levecque, 2010)(Ladwig et al., 2000); we contribute the finding that cognitive ability reduces them further. If educational achievement implies less differentiated gender-based behavior, then our result is consistent with social role model theory. However, since neither education nor cognition eliminated gender differences, our result are also consistent with evolutionary theory.(Costa et al., 2001)(Green & Pope, 1999) We have neither the data nor the inclination to address the relative weight of one theory or another. The simple explanation that we prefer is that women have higher symptom sensitivity, defined as a readiness to perceive sensations as symptoms of illness.(Gijsbers van Wijk, van Vliet, Kolk, & Everaerd, 1991) It appears that higher levels of education and cognition render men more sensitive and women more resilient.

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TABLES & FIGURES

TABLE 1. THE CNT

TEST	ABBREV	FACTOR	SCORE
Verbal Memory Test	VBM	MEM	Correct responses minus errors
Visual Memory Test	VIM	MEM	Correct responses minus errors
Finger Tapping Test	FTT	*	Total number of taps, right and left
Symbol Digit Coding Test	SDC	PS	Correct responses minus errors in two minutes
Stroop Test	RT	PS	Average of complex and Stroop response times
	ST	ATT	Number of errors in non-congruent condition
Shifting Attention Test	SAT	PS	Correct responses minus errors
Continuous Performance Test	CPT	ATT	Correct responses minus errors

*The finger tapping test does not load onto to any of the three factors.

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS

DIAGNOSIS	ALL	M	F	AGE	EDUC	COMFAM	%WHITE
PSYCHIATRIC DISORDERS	**949**	**382**	**567**	**37.09**	**14.13**	**2.69**	**0.77**
Major Depression	327	108	219	39.2	14.4	2.71	0.78
Bipolar Disorder	146	36	110	38.3	14.1	2.73	0.76
Generalized Anxiety	138	52	86	36.3	14.5	2.75	0.83
Post-Traumatic Stress Disorder	72	24	48	39.7	13.7	2.61	0.69
Mood Disorder	67	30	37	34.3	13.6	2.42	0.85
Obsessive-Compulsive Disorder	51	34	17	32.5	15.1	2.88	0.80
Substance Abuse	43	37	6	24.8	12.7	2.85	0.60
Conversion Disorder	35	18	17	44.1	12.5	2.27	0.77
Autism Spectrum	19	14	5	32.1	13.3	2.63	0.74
Schizophrenia	17	7	10	35.5	14.3	2.38	0.59
Social Anxiety	11	9	2	36.3	15.7	2.89	0.91
Alcohol	10	9	1	33.5	14.9	2.80	0.70
Tourettes	6	4	2	20.5	12.0	2.67	1.00
Borderline Personality	5		5	40.6	14.0	3.00	0.40
Eating Disorder	2		2	33.5	14.0	3.00	0.50
NEUROLOGICAL CONDITIONS	**355**	**223**	**132**	**43.64**	**13.98**	**2.46**	**0.81**
Traumatic Brain Injury	215	154	61	43.1	13.5	2.38	0.80
Mild Cognitive Impairment	33	8	25	52.3	14.7	2.70	0.88
Post Concussion Syndrome	21	18	3	41.5	13.9	2.43	0.71
Stroke	18	7	11	48.6	15.8	2.71	0.94
Epilepsy, Seizures	18	5	13	32.4	13.9	2.67	0.67
Dementia	8	5	3	43.6	12.5	2.00	0.75
Parkinsons, Huntingtons	8	6	2	51.0	15.6	2.80	1.00
Multiple Sclerosis	7	1	6	48.3	16.7	2.71	1.00
Encephalitis	6	1	5	38.0	15.3	2.20	1.00
Headache	6	6		38.7	14.6	2.20	0.67
Electrocution	6	5	1	34.2	13.6	2.67	0.50
Mild Brain Injury	3	3		41.3		1.00	1.00
Anoxic Brain Injury, Carbon Monoxide	3	1	2	46.0	16.7	3.00	1.00

Brain Tumor	3	3		46.0		3.00	1.00
COGNITIVE DISORDERS	**452**	**226**	**226**	**43.64**	**13.98**	**2.46**	**0.81**
Attention Deficit Hyperactivity Disorder	432	219	213	30.1	14.6	2.84	0.80
Cognitive Disorder NOS	13	4	9	45.9	14.5	2.69	0.92
Learning Disability	5	3	2	22.8	12.6	2.40	0.80
Subjective Experience Of Cognitive Impairment	2		2	48.5	15.0	2.50	1.00
MEDICAL CONDITIONS	**107**	**50**	**57**	**44.79**	**13.29**	**2.29**	**0.76**
Chronic Pain	90	49	41	45.8	13.1	2.19	0.73
Fibromyalgia	12		12	39.9	14.4	2.92	0.83
Fatigue, Chronic Fatigue	2	1	1	42.5	15.5	3.00	1.00
Cancer	2		2	42.0	14.0	3.00	1.00
Thyroid	1		1	31.0	12.0	2.00	1.00
ALL DIAGNOSES	**1863**	**881**	**982**	**37.20**	**14.16**	**2.66**	**0.79**

TABLE 3. CORRELATIONS OF AVERAGE SYMPTOM SCORE

All Ss	AVGSxS	AGE	EDUC	RACE	COMPNUM	INDEX
AVGSxS	1	.032**	-.297**	.076**	-.228**	-.350**
AGE	.032**	1	.076**	.005	-.285**	-.184**
EDUC	-.297**	.076**	1	-.147**	.442**	.342**
RACE	.076**	.005	-.147**	1	-.107**	-.184**
COMFAM	-.228**	-.285**	.442**	-.107**	1	.380**
INDEX	-.350**	-.184**	.342**	-.184**	.380**	1
Males						
AVGSxS	1	.068**	-.320**	.070**	-.237**	-.337**
AGE	.068**	1	-.037**	-.024**	-.374**	-.217**
EDUC	-.320**	-.037**	1	-.211**	.526**	.354**
RACE	.070**	-.024**	-.211**	1	-.124**	-.204**
COMFAM	-.237**	-.374**	.526**	-.124**	1	.392**
INDEX	-.337**	-.217**	.354**	-.204**	.392**	1
Females						
AVGSxS	1	-.002	-.288**	.078**	-.236**	-.369**
AGE	-.002	1	.180**	.027**	-.200**	-.156**
EDUC	-.288**	.180**	1	-.110**	.328**	.322**
RACE	.078**	.027**	-.110**	1	-.109**	-.177**
COMFAM	-.236**	-.200**	.328**	-.109**	1	.358**
INDEX	-.369**	-.156**	.322**	-.177**	.358**	1

TABLE 4. COGNITIVE PERFORMANCE IN MALES AND FEMALES

	M	F	d	F	Sig.
VBM	47.89	49.91	-0.28	38.173	.000
VIM	43.41	43.65	-0.04	33.032	.000
SDC	44.74	47.56	-0.16	95.715	.000
RT	698.25	685.79	0.07	19.747	.000
SAT	34.22	34.72	-0.02	66.963	.000
ST	29.40	26.70	0.09	6.569	.000
CPT	28.41	32.70	-0.15	2.456	.032
FTT	103.72	96.66	0.21	52.809	.000

TABLE 5. NP3 SCORES, ALL SUBJECTS, BY GENDER

	MALE	SD	FEMALE	SD	d	F	Sig.
AVERAGE SYMPTOM SCORE	82.34	49.68	90.76	48.62	-0.17	39.048	.000
COGNITIVE FACTOR (CF)	117.59	69.75	123.97	70.34	-0.09	56.344	.000
MANIA FACTOR (MF)	71.39	51.84	71.62	49.76	0.00	29.890	.000
SOMATIC FACTOR (SF)	83.45	66.52	101.41	66.17	-0.27	19.202	.000
ANXIETY DEPRESSION FACTOR (ADF)	79.01	57.53	93.40	59.85	-0.24	34.029	.000
FATIGUE (FTG)	124.1	91.2	152.9	90.2	-0.31	18.581	.000
PANIC	57.2	70.6	79.2	80.4	-0.29	18.719	.000
DEPRESSION (DEP)	108.7	76.0	129.7	80.5	-0.26	6.281	.000
ANXIETY (ANX)	120.8	78.3	138.7	77.7	-0.23	31.696	.000
SOMATIC (SOMA)	48.6	54.1	61.2	58.2	-0.22	11.148	.000
AGORAPHOBIA (AGORA)	56.6	62.9	67.7	69.4	-0.17	64.708	.000
PAIN	77.6	77.7	90.2	78.7	-0.16	21.130	.000
MEMORY (MEM)	100.0	71.2	110.6	72.3	-0.15	31.782	.000
ATTENTION (ATT)	142.2	82.5	152.8	83.0	-0.13	28.185	.000
PSYCHOSIS (PSYCH)	56.2	55.0	63.2	58.8	-0.12	19.881	.000
SLEEP	126.5	100.6	138.7	101.9	-0.12	34.198	.000
SOCIAL ANXIETY (SAD)	76.0	70.8	84.6	72.5	-0.12	33.197	.000
OBSESSIONS & COMPULSIONS (OC)	54.7	50.6	60.5	48.5	-0.12	15.846	.000
MOOD STABILITY (MS)	102.5	75.1	110.9	76.0	-0.11	27.898	.000
SUICIDE (SUI)	52.9	73.6	59.1	79.5	-0.08	25.443	.000
HYPERACTIVE-IMPULSIVE (HIP)	98.0	68.7	98.8	66.2	-0.01	14.750	.000
LEARNING PROBLEMS (LPX)	110.6	71.1	108.5	69.9	0.03	42.255	.000
MANIA	50.9	51.1	45.5	49.2	0.11	31.387	.000
AGGRESSION (AGG)	49.3	59.7	39.6	49.5	0.18	25.126	.000
SUBSTANCE ABUSE (SA)	32.6	58.3	22.5	44.0	0.20	4.452	.000

NOTE Table 2. Symptom scales of the anxiety-depression factor are highlighted in yellow. Symptom scales of the somatic factor are highlighted in orange.

TABLE 6. GENDER DIFFERENCES IN ALL PATIENTS AND BY DIAGNOSTIC CATEGORY

ALL		PSYCH		NEURO		COG		DEP		ADD		TBI	
PANIC	**1.37**	**SOMA**	**1.3**	**SUI**	**1.26**	**PANIC**	**1.91**	**PAIN**	**1.30**	**PANIC**	**1.68**	*SA*	*1.49*
SOMA	**1.25**	**PANIC**	**1.24**	**FTG**	**1.25**	**SOMA**	**1.57**	**SOMA**	**1.25**	*PAIN*	*1.28*	**ATT**	**1.29**
FTG	**1.23**	**PAIN**	**1.22**	**ATT**	**1.24**	**PAIN**	**1.43**	**PANIC**	**1.24**	**SOMA**	**1.25**	**FTG**	**1.29**
DEP	**1.19**	**FTG**	**1.22**	**PANIC**	**1.22**	*AGORA*	*1.29*	**FTG**	**1.19**	*FTG*	*1.19*	**LPX**	**1.20**
AGORA	**1.18**	**DEP**	**1.16**	**AGORA**	**1.2**	**FTG**	**1.29**	**AGORA**	**1.17**	*MS*	*1.16*	**MEM**	**1.20**
PAIN	**1.17**	**MEM**	**1.15**	**MEM**	**1.15**	*SAD*	*1.22*	**PSYCH**	**1.17**	**ANX**	**1.16**	**AGORA**	**1.17**
ANX	**1.16**	**AGORA**	**1.14**	**ANX**	**1.13**	**OC**	**1.2**	*DEP*	*1.12*	**DEP**	**1.14**	**ANX**	**1.12**
OC	**1.14**	**ANX**	**1.12**	**DEP**	**1.12**	**ANX**	**1.19**	**MEM**	**1.12**	**OC**	**1.13**	**PANIC**	**1.12**
SAD	**1.11**	**SLEEP**	**1.11**	*SA*	*1.11*	**PSYCH**	**1.19**	**MS**	**1.10**	**PSYCH**	**1.10**	*DEP*	*1.10*
PSYCH	**1.11**	**OC**	**1.09**	**SLEEP**	**1.11**	**DEP**	**1.18**	**SLEEP**	**1.10**	**MEM**	**1.09**	*SUI*	*1.09*
SLEEP	**1.1**	**PSYCH**	**1.08**	**SAD**	**1.1**	MS	1.15	**ATT**	**1.08**	*SAD*	*1.09*	**SAD**	**1.04**
MEM	**1.1**	**ATT**	**1.08**	**SOMA**	**1.07**	**MEM**	**1.12**	**ANX**	**1.05**	**AGORA**	**1.08**	**HIP**	**1.02**
ATT	**1.09**	**MS**	**1.06**	**LPX**	**1.06**	*HIP*	*1.07*	**OC**	**1.05**	*HIP*	*1.08*	**SLEEP**	**1.00**
MS	**1.07**	*SUI*	*1.05*	**PAIN**	**1.02**	*SLEEP*	*1.07*	**LPX**	**1.04**	*ATT*	*1.03*		
SUI	**1.07**	**SAD**	**1.04**			**ATT**	**1.03**	**SAD**	**1.04**			**MANIA**	**0.99**
HIP	**1.02**			**HIP**	**1**					**LPX**	**0.97**	**SOMA**	**0.98**
		LPX	**1**	**PSYCH**	**0.99**	**LPX**	**0.99**	***SUI***	***1.00***	*SLEEP*	*0.96*	*OC*	*0.98*
LPX	**1**	**HIP**	**0.98**	**OC**	**0.98**	**SUI**	**0.95**	**HIP**	**0.96**	**SUI**	**0.93**	**PAIN**	**0.96**
MANIA	**0.89**	**MANIA**	**0.85**	**MS**	**0.89**	**MANIA**	**0.84**	**AGG**	**0.95**	**AGG**	**0.79**	**MS**	**0.90**
AGG	**0.79**	**AGG**	**0.78**	**MANIA**	**0.87**	**AGG**	**0.74**	**MANIA**	**0.89**	**MANIA**	**0.77**	**PSYCH**	**0.84**
SA	**0.68**	**SA**	**0.64**	**AGG**	**0.72**	**SA**	**0.51**	*SA*	*0.56*	*SA*	*0.58*	**AGG**	**0.62**

NOTE, Table 3. Scales in the anxiety-depression and somatic factors are highlighted as in Table 2. Scale scores that are significantly different at the P < 0.01 level are in bold. Scales that do not show gender differences are in italic.

FIGURES 1A AND 1B. GENDER DIFFERENCES IN 20 SYMPTOM SCALE SCORES AND DIFFERENCES BY HIGH AND LOW EDUCATION/COGNITION

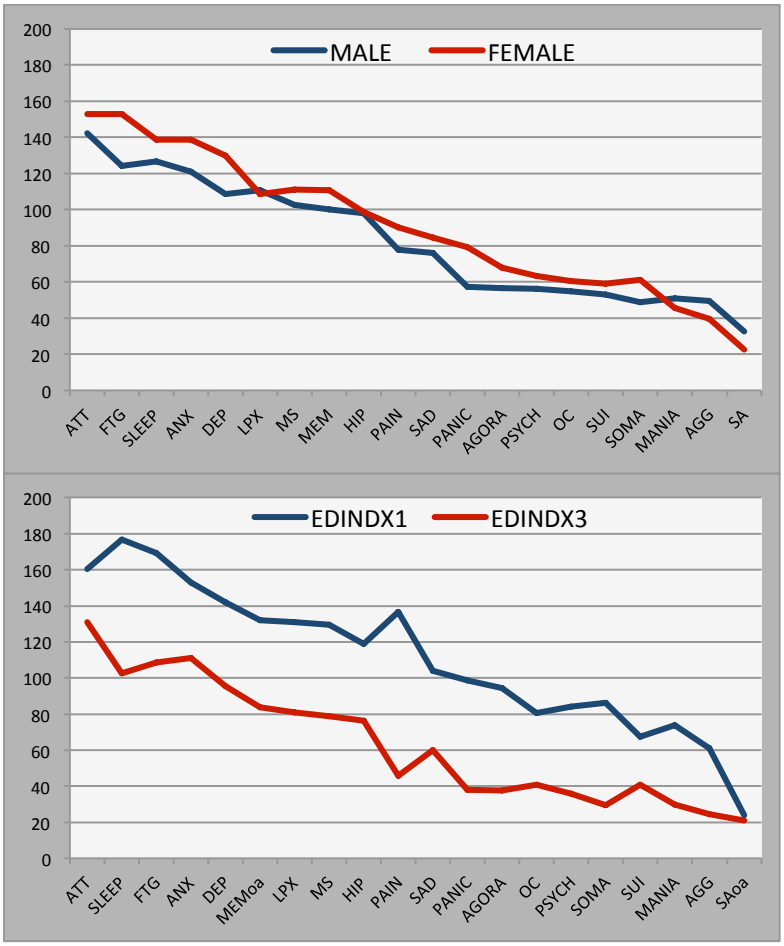
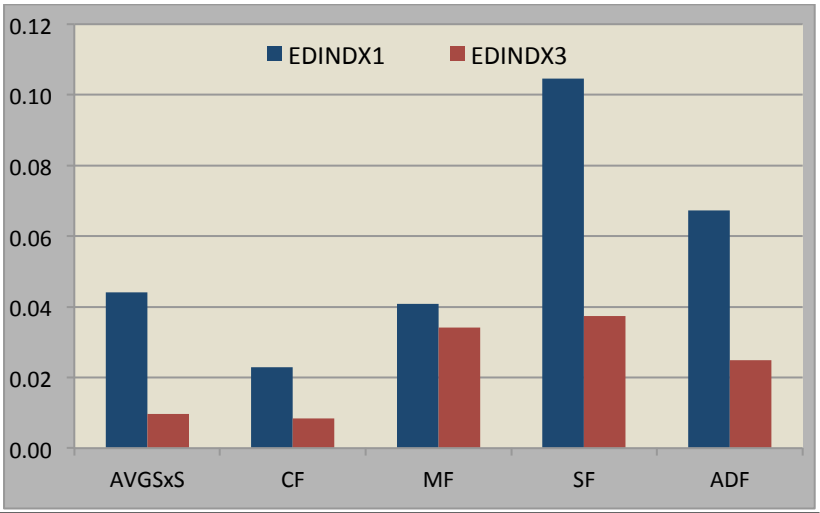


FIGURE 2. GENDER DIFFERENCES IN LOW AND HIGH EDUCATION/COGNITION GROUPS



Note, Figure 2. The y axis is partial *eta* squared, an effect size measure that captures the variance in symptom scores attributable to gender differences.