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Associations between aspects of pain and cognitive performance and the contribution of depressive symptoms in mid-life women: A cross-sectional analysis

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Abstract

Objectives—Pain has been associated with cognitive problems in pain patients. This study evaluated the extent to which experiences of pain are associated with cognitive performance in a community sample of mid-life women, and the contribution of depressive symptoms to this association.

Study Design—A cross-sectional analysis was used with data from the Study of Women's Health Across the Nation (SWAN). Associations between aspects of pain and cognitive performance were evaluated using statistical models with and without depressive symptoms.

Main Outcome Measures—The cognitive performance score was a composite of three cognitive tests, the Digit Span Backward Test, the Symbol Digit Modalities Test and the East Boston Memory Test.

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I will follow up with an email attachment of the ethical approval from the SWAN Study. <http://www.swanstudy.org/>

The contributors and their roles are listed in the cover letter.

Competing interests are listed in the cover letter.

Results—Greater pain experiences that interfered with daily work were independently associated with poorer cognitive performance, [β (SE) -0.074 (0.021); p value <0.01] and this association was partially explained by depressive symptoms [β (SE) -0.061 (0.022); p value <0.01 after adjusting for depressive symptoms]. Additionally, an independent association between a greater composite pain score and poorer cognitive performance was identified without adjusting for depressive symptoms, [β (SE) -0.002 (0.0009); p value <0.05] but was no longer significant after adjusting for depressive symptoms.

Conclusions—Our results suggest that in mid-life women, greater pain is associated with poorer cognitive performance, and depressive symptoms play an important role in this association. Clinicians should be aware of these relationships when evaluating patients.

Keywords

Pain; cognitive function; depressive symptoms

1. Introduction

Chronic pain has been associated with cognitive problems in the domains of memory, concentration, problem solving, abstract thinking, and cognitive efficiency¹⁻³. Most evidence related to the adverse effect of pain on cognitive functioning is derived from chronic pain patients, including those with fibromyalgia, whiplash, arthritis and other chronic pain conditions⁴⁻⁷. It is unclear whether general pain experiences affect cognitive function in the middle-aged and older adult population. This question is important because general pain experiences occur in a substantial proportion of middle-aged and older adults⁸.

In the few studies of pain and cognitive function in general community samples, findings are mixed⁹⁻¹². A study of middle-aged and older European men, for example, found that those reporting pain in multiple areas of the body and lasting at least 3 months had poorer cognitive function compared to those who were pain free¹¹. Another study found that community-dwelling older adults with intense low back pain lasting at least 3 months had poorer cognitive function compared with those reporting no pain¹⁰. In contrast, a study of Swedish adults failed to find a significant association between pain in various parts of the body (e.g. back, arms, legs) and cognitive function¹². The research in general community samples is too scarce to draw conclusions about pain-cognition relationships, and further, it is not clear whether every aspect of pain (for example, duration or intensity) relates to cognitive performance similarly or if certain aspects of pain are more related than others.

Pain can lead to greater depressive symptoms¹³, and those with depressive symptoms are more likely to have poorer cognitive function¹⁴; due to these links, depression has been conceptualized as a mediator in the association between pain and cognitive function^{11,15}. Cross-sectional studies reporting that associations between pain and cognitive performance are attenuated after adjusting for depression^{11,15} have either included patients selected based on painful chronic health conditions¹⁵ or have evaluated a chronic widespread pain condition¹¹, which may not represent the nature of pain that is frequently experienced in the general population. No studies of pain, cognition and depressive symptoms to date have focused specifically on women, but they are needed because women experience pain

differently than men¹⁶ and because depression is an important consideration for midlife women¹⁷.

The present study investigates the relationship between pain and cognitive performance in a large, community-dwelling sample of mid-life women. We focus on two distinct aspects of the pain experience: pain intensity and pain-related interference with work, which have not been well characterized in relation to cognitive performance. We hypothesize that higher levels of pain intensity and greater pain-related interference with work are associated with poorer cognitive performance. We also evaluate the contribution of depressive symptoms to these associations.

2. Materials and Methods

2.1. Sample and procedures

Participants are from the Study of Women's Health Across the Nation (SWAN), a multisite, multiethnic longitudinal study of women at midlife established to characterize the health of women as they approach and traverse the menopausal transition. The study design and recruitment for SWAN have been described¹⁸. Eligibility criteria included being aged 42–52 years, having an intact uterus, having had at least one menstrual period and no use of reproductive hormones in the previous 3 months, and self-identifying with a study site's designated race/ethnic groups. Each of the seven study sites recruited approximately 450 participants (total $n = 3,302$). All sites enrolled non-Hispanic whites, and each site also enrolled women in one specified minority ethnic group. African-American women were enrolled in Boston, Chicago, Southeast Michigan, and Pittsburgh. Japanese, Chinese, and Hispanic women were enrolled in Los Angeles and Oakland, California, and in Hudson County, New Jersey, respectively. All women were either premenopausal or early perimenopausal at the baseline visit. Women were assessed at baseline and annually with a similar protocol that included self-report and interviewer administered questionnaires regarding multiple psychosocial, biological, lifestyle and health domains including physical measures. Study questionnaires were translated into Cantonese, Japanese and Spanish. Approval by the Institutional Review Board was granted and informed consent was obtained from each study participant. The analytic sample is from the 8th annual SWAN follow up visit, which was conducted in 2004 and 2005. The visit 8 time point was selected because the entire set of variables proposed for analysis was available at or very near this time point. Hispanic and white participants from the New Jersey site were not included in this analysis because no data are available for this group at the visit 8 time point. The final analytic sample included 1413 participants.

2.2. Measures

2.2.1. Cognitive Performance—The SWAN study included three tests of cognitive performance commonly used in research of community-dwelling adults. The Digit Span Backward Test was used as a measure of working memory¹⁹, the Symbol Digit Modalities Test was used to assess processing speed²⁰, and the East Boston Memory Test was used to evaluate verbal episodic memory, with separate scores for immediate and delayed recall²¹.

2.2.2. Aspects of pain and depressive symptoms—Aspects of pain were assessed with the bodily pain scale from the MOS 36-Item Short-Form Health Survey (SF-36)²². This scale assesses pain severity during the past 4 weeks (none, very mild, mild, moderate, severe, or very severe), and how much pain interfered with normal work including work outside the home and housework (not at all, slightly, moderately, quite a bit, or extremely). We used scores from each question separately, as well as the combined SF-36 bodily pain subscale in which raw scores were rescaled to a range of 0-100 points²³. Separate analyses allowed us to evaluate whether severity and/or impact of pain on functioning might be differentially associated with cognitive performance. The SF-36 scores are presented on their original scale (*higher* score indicating less pain) in the descriptive results but they are reversed for modeling (*lower* score indicating less pain). Depressive Symptoms were assessed using the Center for Epidemiologic Studies Depression (CESD) Scale²⁴, a 20-item questionnaire that asks about the frequency of being bothered by depressive symptoms during the previous week on a scale of 0 (rarely) to 3 (most or all of the time) for a total summed score ranging from 0-60. This scale was developed to assess depressive symptoms in epidemiological studies and has been shown to be valid and reliable in diverse ethnic populations²⁵⁻²⁷.

2.2.3. Covariates—Demographic information, menstrual bleeding and medication use were self-reported via questionnaire. Economic hardship was characterized by asking respondents how hard it was to pay for basics like food, housing, medical care, and heating (adapted from Pearlin²⁸). Menopausal transition stage was based on annual reports of menstrual bleeding. Premenopause was identified as no decreased regularity in menstrual bleeding during the previous year. Other classifications were early perimenopause (menses in the past 3 months and decreased menses regularity in the 12 months before the interview), late perimenopause (no menses for 3–11 months), and postmenopause (no menses for 12 or more months). Surgical menopause was defined by report of either hysterectomy or oophorectomy. The “undeterminable status” category was comprised of pre- and perimenopausal women using hormones.

Prescription and over-the-counter pain medications taken at least twice per week in the last month were reported and captured as yes/no current use. Pain medication use was classified as: (1) prescription opioid-based medications; (2) prescription and over-the-counter non-opioid-based pain medications; or (3) no pain medications. If an individual reported taking both opioid-based and non-opioid-based medication, she was classified into the opioid pain medication category since that category is most likely to impact cognitive function. One individual reporting low-dose (81mg) aspirin use was classified as taking no pain medications as it is below an effective dose for pain.

2.3 Statistical analyses

In a principal-components factor analysis, the four cognitive performance scores loaded on a single factor that accounted for approximately 93% of the variance in the individual tests. Therefore, we formed a composite measure of cognition by converting raw scores for each of the tests to z scores (using the mean and SD for each), and then averaged the z scores to get the composite score. This approach has been used previously²⁹. If fewer than four

cognitive test scores were available, available scores were averaged. Higher scores indicate better cognitive performance. Correlations among the three pain variables were estimated using Spearman rank correlation coefficients.

To obtain estimates of adjusted associations, ordinary least squares regression models were used. Potential confounders and covariates were based on the literature and a priori hypotheses. Race/ethnicity, age, economic hardship and education level are risk factors for pain³⁰ and cognitive performance^{31,32}. Additionally, menopausal transition stage and pain medication use are associated with pain^{33,34} and cognitive function^{31,35,36}.

To evaluate the association between pain and cognitive performance independent of depressive symptoms, two models were run for each pain variable: model 1 adjusted for demographic confounders including age (centered at 55 years), race/ethnicity (non-Hispanic white is the reference group), education level (some college is the reference group), economic hardship (no trouble paying for basics is the reference group), and study site (Los Angeles is the reference group) and model 2 adjusted for more proximal confounders including all variables in model 1 plus menopausal transition stage (combined early and late peri-menopause categories are the reference group) and pain medications. A third set of models included covariates from models 1 and 2 but further adjusted for depressive symptoms (included as a continuous variable). We evaluated the contribution of depressive symptoms to the pain-cognitive performance association by comparing the magnitude of associations between aspects of pain and cognitive performance in models 2 and 3 (i.e. models with and without depressive symptoms). For statistical modeling, a higher score indicates *more* pain. Pain severity and pain interference were modeled as ordinal variables. A 2-sided p value equal to or less than 0.05 was considered significant and >0.05 to less than 0.1 was considered borderline significant. Data analysis was performed in SAS version 9.3.

3. Results

Most of the 1,413 women in this sample of SWAN participants were in their fifties [median (IQR) age 53 (4) years; Table 1]. Just over half were non-Hispanic white, over a quarter were African American, and the rest were Chinese (10%) and Japanese (12%), reflecting the original recruitment design of SWAN. Only a small minority of participants found it very hard (5%) to pay for basics like food, housing, medical care and heating, but 21% found it somewhat hard to pay for these types of items. Half the participants had not received a college degree, including about 3% who did not complete high school, 16% who completed high school or equivalent and 32% with some college. More than half of the sample was postmenopausal (51.1%) or surgically postmenopausal (6.7%).

Almost half (49%) of the participants reported pain of at least mild intensity during the 4 weeks. About a quarter experienced at least moderate pain, with 5.5 % reporting severe to very severe pain. Just under half (44.4%) of participants reported some interference in their work from pain with 10.2% indicating that pain interfered moderately and 5.9% reporting that pain interfered quite a bit or extremely. The median (IQR) SF36 bodily pain score was 74 (23), where a score of 100 indicates the least pain. Two percent (2%) of participants reported taking opioid-based pain medication and 21% of participants reported taking non-

opioid-based medications for pain at least twice a week in the past month. The correlation between pain intensity and interference from pain was moderately strong ($r=0.66$; $p<0.0001$; not shown).

Higher SF-36 combined bodily pain score (reverse scored in models so that higher scores indicate more pain) was significantly associated with lower cognitive score in models 1 and 2 [β (SE) -0.0023 (0.0008), $p=0.006$; and β (SE) -0.0019 (0.0009), $p=0.04$, respectively, rounded for presentation in Table 2]. Greater intensity of bodily pain was borderline significantly associated with the cognitive score in model 1 [β (SE) -0.026 (0.016); $p=0.09$] indicating that for each higher level of pain intensity, there was a -0.026 decrease in the cognitive score. This association was no longer significant in model 2. The association between greater interference from pain and lower cognitive score was significant in model 1 [β (SE) -0.082 (0.020); $p<0.0001$], and remained significant after inclusion of additional covariates (model 2).

After further adjusting models for depressive symptoms (model 3), only the association between greater interference from pain and lower cognitive score remained significant, though the parameter estimate diminished 24% compared to model 2 (from -0.074 to -0.061 , Tables 2 and 3). Depressive symptoms was significantly associated with cognitive performance in separate models adjusting for SF-36 score [β (SE) -0.006 (0.002), $p=0.02$], intensity of pain [β (SE) -0.006 (0.002), $p=0.007$], and interference from pain [β (SE) -0.005 (0.002), $p=0.04$] (Table 3, model 3).

4. Discussion

We found that a substantial proportion of middle-aged women experienced pain: about one in four reported at least moderate intensity of pain during the past 4 weeks, and about one in six reported that pain interfered at least moderately with their usual activities at work or at home. Worse SF-36 composite pain scores and greater pain experiences that interfered with daily functioning at work or at home were associated with poorer cognitive performance independent of potential confounders, including menopausal transition stage and use of pain medication. Depressive symptoms explained some of the association between cognitive performance and pain that interfered with functioning and all of the association with the composite pain score.

Pain was a fairly common experience for many participants in our sample but as expected, the intensity of the pain was generally mild, and normative data show that pain is even more problematic in US midlife women²³ compared to our sample. The amount of pain our participants reported, reflected in the SF-36 pain subscale [mean (SD) 74.0 (23.1)], is slightly better compared to US females aged 45-54 years [mean (SD) 72.1 (23.3)]²³.

Pain is often referred to as a high priority signal, and it is thought to slow, stop or impair behavior when cognitive demand is high³⁷. In the brain, somatosensory relay nuclei in the thalamus receive ascending spinothalamic projections and relay nociceptive information to the somatosensory cortices. These somatosensory cortices, which interconnect anatomically with the corticolimbic somatosensory pathway, integrate somatosensory input with learning

and memory functions³⁸. Using MRI to measure whole brain gray matter volume, Apkarian et al³⁹ observed that chronic back pain was associated with reduced gray matter in thalamocortical areas. Thus, reductions in thalamic and cortical gray matter may correlate with decreased pain inhibition as well as contribute to cognitive symptoms observed in chronic pain disorders, including a decreased ability to process information required for cognitive tasks.

We extended existing research suggesting that depressive symptoms play a role in the pain-cognitive performance relationship by evaluating the contribution of depressive symptoms in this community-based sample of midlife women. Our analyses showed that once depressive symptoms were accounted for, the association between the SF-36 combined pain score and cognitive performance was no longer significant; in other words, depressive symptoms explained the entire association. Depressive symptoms only explained part of the association with interference from pain, however. Because of our cross-sectional study design, we were unable to distinguish whether depressive symptoms were confounding or mediating these associations, or acting through both of these pathways.

Nevertheless, some cross-sectional studies have performed mediation analysis, which suggest that depressive symptoms may mediate between chronic pain and cognitive performance^{15,11}. Though little is known about pain that is not chronic, it has been shown that depressive symptoms influence the intensity of pain¹³. Further, research suggests that pain catastrophizing may be an important link in the pathway from pain to depressive symptoms⁴⁰. This is relevant to our results because the experience of pain may be different for men and women; women reportedly catastrophize more than men in response to pain¹⁶. Additionally, depressive symptoms may have detrimental effects on cognitive performance⁴¹ possibly because psychological distress engages resources that are required for cognitive tasks¹⁵, including attention⁴¹. More research examining longitudinal associations among specific pain aspects, depressive symptoms and cognitive performance are needed to clarify the role of depressive symptoms and may provide insight into pathways bridging pain and cognitive performance. This information will be relevant to clinicians who may need to consider pain experiences in those with depressive symptoms in order to promote cognitive health.

The SWAN study offers many strengths, including rich information on different aspects of the pain experience in a multi-ethnic sample, providing an excellent opportunity to investigate how pain might relate to cognitive performance in a community-based sample. Our findings contribute new information which is particularly relevant to women as they are more sensitive to pain compared to men, and because the midlife in particular often presents cognitive challenges for women⁴². It is important to acknowledge the limitations of this study by emphasizing that the cross-sectional design limits causal inference; there is no way to distinguish between mediation and confounding with cross-sectional data, regardless of the analytic approach. Further, our measures of pain did not capture chronic pain and only reflect the prior four weeks. Our research question is intended to address the pain experienced in a general sample of women, which likely include some people with chronic pain as well as some who experience pain that is not chronic.

5. Conclusion

Pain and cognitive performance are important and relatively common concerns for midlife women. This study provided information on the direction and significance of associations. Clinicians should be aware of the relationships between cognitive performance and different aspects of pain, and the role of depressive symptoms so that they can appropriately evaluate and treat patients.

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References

1. McCracken LM, Iverson GL. Predicting complaints of impaired cognitive functioning in patients with chronic pain. *Journal of pain and symptom management*. May; 2001 21(5):392–396. [PubMed: 11369160]
2. Schnurr RF, MacDonald MR. Memory complaints in chronic pain. *The Clinical journal of pain*. Jun; 1995 11(2):103–111. [PubMed: 7549165]
3. Iezzi T, Archibald Y, Barnett P, Klinck A, Duckworth M. Neurocognitive performance and emotional status in chronic pain patients. *Journal of behavioral medicine*. Jun; 1999 22(3):205–216. [PubMed: 10422614]
4. Verdejo-Garcia A, Lopez-Torrecillas F, Calandre EP, Delgado-Rodriguez A, Bechara A. Executive function and decision-making in women with fibromyalgia. *Archives of clinical neuropsychology: the official journal of the National Academy of Neuropsychologists*. Feb; 2009 24(1):113–122. [PubMed: 19395361]

5. Antepohl W, Kiviloog L, Andersson J, Gerdle B. Cognitive impairment in patients with chronic whiplash-associated disorder--a matched control study. *NeuroRehabilitation*. 2003; 18(4):307–315. [PubMed: 14757927]
6. Bosma FK, Kessels RP. Cognitive impairments, psychological dysfunction, and coping styles in patients with chronic whiplash syndrome. *Neuropsychiatry, neuropsychology, and behavioral neurology*. Mar; 2002 15(1):56–65.
7. Jorge LL, Gerard C, Revel M. Evidences of memory dysfunction and maladaptive coping in chronic low back pain and rheumatoid arthritis patients: challenges for rehabilitation. *European journal of physical and rehabilitation medicine*. Dec; 2009 45(4):469–477. [PubMed: 20032904]
8. American Pain Foundation. Overview of American pain surveys: 2005-2006. *Journal of pain & palliative care pharmacotherapy*. 2008; 22(1):33–38. [PubMed: 19062352]
9. Gijzen CP, Dijkstra JB, van Boxtel MP. Recurrent pain is associated with decreased selective attention in a population-based sample. *Pain*. Jan; 2011 152(1):188–193. [PubMed: 21122991]
10. Weiner DK, Rudy TE, Morrow L, Slaboda J, Lieber S. The relationship between pain, neuropsychological performance, and physical function in community-dwelling older adults with chronic low back pain. *Pain medicine*. Jan-Feb; 2006 7(1):60–70. [PubMed: 16533199]
11. Lee DM, Pendleton N, Tajar A, et al. Chronic widespread pain is associated with slower cognitive processing speed in middle-aged and older European men. *Pain*. Oct; 2010 151(1):30–36. [PubMed: 20646831]
12. Soderfjell S, Molander B, Johansson H, Barnekow-Bergkvist M, Nilsson LG. Musculoskeletal pain complaints and performance on cognitive tasks over the adult life span. *Scandinavian journal of psychology*. Oct; 2006 47(5):349–359. [PubMed: 16987204]
13. Torta RG, Munari J. Symptom cluster: Depression and pain. *Surgical oncology*. Sep; 2010 19(3): 155–159. [PubMed: 20106657]
14. Baune BT, Miller R, McAfoose J, Johnson M, Quirk F, Mitchell D. The role of cognitive impairment in general functioning in major depression. *Psychiatry research*. Apr 30; 2010 176(2-3):183–189. [PubMed: 20138370]
15. Brown SC, Glass JM, Park DC. The relationship of pain and depression to cognitive function in rheumatoid arthritis patients. *Pain*. Apr; 2002 96(3):279–284. [PubMed: 11973000]
16. Jensen I, Nygren A, Gamberale F, Goldie I, Westerholm P. Coping with long-term musculoskeletal pain and its consequences: is gender a factor? *Pain*. May; 1994 57(2):167–172. [PubMed: 8090513]
17. Centers for Disease Control and Prevention. Current depression among adults---United States, 2006 and 2008. *MMWR. Morbidity and mortality weekly report*. Oct 1; 2010 59(38):1229–1235. [PubMed: 20881934]
18. Sowers, MFCS.; Sternfeld, B.; Morgenstein, D.; Gold, E.; Greendale, G.; Evans, D.; Neer, R.; Matthews, K.; Sherman, S.; Lo, A.; Weiss, G.; Kelsey, J. Menopause: biology and pathobiology. In: Lobo, RAKJ.; Marcus, R., editors. *Menopause: biology and pathobiology*. Academic Press; New York, NY: 2000. p. 175-188.
19. The Psychological Corporation. WAIS-III and WMS-III: Technical manual. Psychological Corporation/ Harcourt Brace; San Antonio, TX: 1997.
20. Smith, A. Symbol Digit Modalities Test. Western Psychological Service; Los Angeles, CA: 1982.
21. Wechsler D. A standardized memory scale for clinical use. *Psychology*. 1945; 19:87–95.
22. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical care*. Jun; 1992 30(6):473–483. [PubMed: 1593914]
23. Ware, JE, Jr.. SF-36 Health Survey. Manual and Interpretation Guide. The Health Institute, New England Medical Center; Boston, MA: 1993.
24. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1:385–401.
25. Guarnaccia PJ, Angel R, Worobey JL. The factor structure of the CES-D in the Hispanic Health and Nutrition Examination Survey: the influences of ethnicity, gender and language. *Social science & medicine*. 1989; 29(1):85–94. [PubMed: 2740931]
26. Jones-Webb RJ, Snowden LR. Symptoms of depression among blacks and whites. *American journal of public health*. Feb; 1993 83(2):240–244. [PubMed: 8427330]

27. Ying YW. Depressive symptomatology among Chinese-Americans as measured by the CES-D. *Journal of clinical psychology*. Sep; 1988 44(5):739–746. [PubMed: 3192712]
28. Pearlin LI, Lieberman MA, Menaghan EG, Mullan JT. The stress process. *Journal of health and social behavior*. Dec; 1981 22(4):337–356. [PubMed: 7320473]
29. Barnes LL, Mendes de Leon CF, Bienias JL, Wilson RS, Everson-Rose SA, Evans DA. Hostility and change in cognitive function over time in older blacks and whites. *Psychosomatic medicine*. Jul; 2009 71(6):652–658. [PubMed: 19483119]
30. Medicine, Io. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington (DC): 2011.
31. Hendrie HC, Albert MS, Butters MA, et al. The NIH Cognitive and Emotional Health Project. Report of the Critical Evaluation Study Committee. *Alzheimer's & dementia: the journal of the Alzheimer's Association*. Jan; 2006 2(1):12–32.
32. Wadley VG, Unverzagt FW, McGuire LC, et al. Incident cognitive impairment is elevated in the stroke belt: the REGARDS study. *Annals of neurology*. Aug; 2011 70(2):229–236. [PubMed: 21618586]
33. Rolita L, Freedman M. Over-the-counter medication use in older adults. *Journal of gerontological nursing*. Apr; 2008 34(4):8–17. [PubMed: 18429375]
34. Manson JE. Pain: sex differences and implications for treatment. *Metabolism: clinical and experimental*. Oct; 2010 59(Suppl 1):S16–20. [PubMed: 20837187]
35. Greendale GA, Wight RG, Huang MH, et al. Menopause-associated symptoms and cognitive performance: results from the study of women's health across the nation. *American journal of epidemiology*. Jun 1; 2010 171(11):1214–1224. [PubMed: 20442205]
36. Hart RP, Martelli MF, Zasler ND. Chronic pain and neuropsychological functioning. *Neuropsychology review*. Sep; 2000 10(3):131–149. [PubMed: 10983898]
37. Eccleston C. Chronic pain and attention: a cognitive approach. *The British journal of clinical psychology / the British Psychological Society*. Nov; 1994 33(Pt 4):535–547. [PubMed: 7874045]
38. Price DD. Psychological and neural mechanisms of the affective dimension of pain. *Science*. Jun 9; 2000 288(5472):1769–1772. [PubMed: 10846154]
39. Apkarian AV, Sosa Y, Sonty S, et al. Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. *The Journal of neuroscience: the official journal of the Society for Neuroscience*. Nov 17; 2004 24(46):10410–10415. [PubMed: 15548656]
40. Buenaver LF, Edwards RR, Smith MT, Gramling SE, Haythornthwaite JA. Catastrophizing and pain-coping in young adults: associations with depressive symptoms and headache pain. *J Pain*. Apr; 2008 9(4):311–319. [PubMed: 18165160]
41. Baune BT, Miller R, McAfoose J, Johnson M, Quirk F, Mitchell D. The role of cognitive impairment in general functioning in major depression. *Psychiatry Res*. Apr 30; 2010 176(2-3):183–189. [PubMed: 20138370]
42. Dugan SA, Powell LH, Kravitz HM, Everson Rose SA, Karavolos K, Luborsky J. Musculoskeletal pain and menopausal status. *Clin J Pain*. May; 2006 22(4):325–331. [PubMed: 16691084]

Highlights

- We evaluated associations between pain, cognitive performance and depressive symptoms
- Greater pain interfering with daily work was associated with poorer cognitive performance.
- A greater composite pain score was associated with poorer cognitive performance.
- Depressive symptoms played an important role in these associations.

Table 1

Descriptive characteristics of female SWAN participants in 2004/2005 (n=1413)

Characteristic	Median (IQR) or Frequency (%)
Age in years: median (IQR) ^a	53 (4)
Race/ethnicity: Frequency (%)	
African American	382 (27)
White	733 (52)
Chinese	136 (10)
Japanese	162 (11)
Economic hardship ^b : Frequency (%)	
Paying for basics very hard	63 (5)
Paying for basics somewhat hard	285 (21)
Paying for basics not hard at all	1031 (75)
Education: Frequency (%)	
Less than high school	39 (3)
Completed high school / GED	223 (16)
Some college/ tech school	443 (32)
College degree	322 (23)
Post graduate degree	381 (27)
Menopausal transition stage: Frequency (%)	
Premenopausal	22 (2)
Early peri-menopausal	330 (23)
Late peri-menopausal	179 (13)
Post menopausal	722 (51)
Surgically postmenopausal	94 (7)
Status undeterminable ^c	65 (5)
Pain intensity during the past 4 weeks: Frequency (%)	
None	222 (16)
Very Mild	484 (35)
Mild	326 (24)
Moderate	277 (20)
Severe or Very Severe	76 (6)
How much pain interfered with work in past 4 weeks: Frequency (%)	
Not at all	768 (56)
Slightly	392 (28)
Moderately	141 (10)
Quite a bit or Extremely	82 (6)

Characteristic	Median (IQR) or Frequency (%)
SF-36 bodily pain score ^d : median (IQR)	74 (23)
Pain medications ^e : Frequency (%)	
Took prescription opioid-based pain medications at least 2 times per week in past month	28 (2)
Took prescription or over-the-counter non-opioid-based pain medications at least 2 times per week in past month	303 (21)
Had not taken prescription or over-the-counter pain medication at least 2 times per week in past month	1082 (77)
CES-D score: median (IQR) ^a	5 (9)

^a IQR= interquartile range; GED=General equivalency diploma

^b “Basics” in the economic hardship variable include food, housing, medical care, and heating

^c “Status undeterminable” consisted of pre- and perimenopausal women using hormones

^d A higher SF-36 score is interpreted as less pain (total possible range 1-100 points)

^e If an individual was taking both opioid and non-opioid-based pain medication, she was classified as taking opioid-based pain medication (categories are mutually exclusive).

Table 2

Cross-sectional associations between each pain measure and the overall cognitive performance outcome without consideration of depressive symptoms, Study of Women's Health Across the Nation, 2004-2005^a

	SF-36 bodily pain score ^b		Intensity of pain ^b		Interference from pain ^b	
Variable	Model 1 [β (SE)]	Model 2 [β (SE)]	Model 1 [β (SE)]	Model 2 [β (SE)]	Model 1 [β (SE)]	Model 2 [β (SE)]
Pain measure listed in column	-0.002 (0.0008)**	-0.002 (0.0009)*	-0.026 (0.016)	-0.017 (0.016)	-0.082 (0.020)***	-0.074 (0.021)**
Age (years)	-0.009 (0.007)	-0.007 (0.007)	-0.001 (0.007)	-0.008 (0.007)	-0.008 (0.007)	-0.006 (0.007)
Race/ethnicity ^c						
African American	-0.400 (0.045)***	-0.398 (0.045)***	-0.400 (0.045)***	-0.400 (0.045)***	-0.391 (0.045)***	-0.391 (0.045)***
Chinese	-0.140 (0.082)	-0.152 (0.082)	-0.141 (0.083)	-0.153 (0.083)	-0.115 (0.082)	-0.129 (0.082)
Japanese	-0.119 (0.074)	-0.129 (0.075)	-0.115 (0.075)	-0.127 (0.075)	-0.121 (0.074)	-0.130 (0.074)
Socioeconomic variables						
Economic hardship	-0.119 (0.034)**	-0.112 (0.034)**	-0.129 (0.034)**	-0.120 (0.034)**	-0.105 (0.034)**	-0.098 (0.034)**
Education level	0.124 (0.016)***	0.122 (0.016)***	0.124 (0.016)***	0.122 (0.016)***	0.125 (0.016)***	0.124 (0.016)***
Study site ^d						
Michigan	-0.100 (0.074)	-0.094 (0.074)	-0.107 (0.074)	-0.099 (0.074)	-0.096 (0.074)	-0.090 (0.074)
Boston	-0.197 (0.071)**	-0.195 (0.072)**	-0.194 (0.071)**	-0.191 (0.072)**	-0.206 (0.071)**	-0.204 (0.071)**
Chicago	-0.049 (0.078)	-0.052 (0.079)	-0.046 (0.079)	-0.049 (0.079)	-0.057 (0.078)	-0.059 (0.078)
Davis	-0.022 (0.082)	-0.023 (0.083)	-0.023 (0.083)	-0.025 (0.083)	-0.028 (0.082)	-0.026 (0.082)
Pittsburgh	0.057 (0.070)	0.057 (0.070)	0.059 (0.070)	0.060 (0.070)	0.051 (0.070)	0.051 (0.070)
Menopausal transition stage ^e						
Premenopausal		0.298 (0.136)*		0.295 (0.136)*		0.304 (0.135)*
Post menopausal		0.007 (0.041)		0.007 (0.041)		0.008 (0.041)
Surgically postmenopausal		-0.097 (0.072)		-0.100 (0.073)		-0.093 (0.072)
Status undeterminable ^f		-0.024 (0.086)		-0.026 (0.086)		-0.022 (0.085)
Pain medications ^g						
Opioid-based pain medication ^h		0.207 (0.125)		-0.247 (0.124)*		-0.170 (0.124)

	SF-36 bodily pain score ^b		Intensity of pain ^b		Interference from pain ^b	
Variable	Model 1 [β (SE)]	Model 2 [β (SE)]	Model 1 [β (SE)]	Model 2 [β (SE)]	Model 1 [β (SE)]	Model 2 [β (SE)]
Non-opioid-based pain medication ^h		-0.024 (0.044)		-0.037 (0.044)		-0.016 (0.043)

^a*P value<0.05 **P value <0.01 ***P value <0.001

^b A higher score is interpreted as more pain

^c The reference group for race/ethnicity is non-Hispanic white

^d The reference group for site is the Los Angeles study site

^e The reference group for menopausal transition stage is peri-menopause

^f“Status undeterminable” consisted of pre- and perimenopausal women using hormones

^g The reference group for pain medication is had not taken prescription or over-the-counter pain medication at least 2 times per week in past month

^h Took medication at least 2 times per week in past month

Table 3

Cross-sectional associations between each pain measure and the overall cognitive performance outcome after adjustment for depressive symptoms, Study of Women's Health Across the Nation, 2004-2005^a

Variable	SF-36 bodily pain score ^b	Intensity of pain ^b	Interference from pain ^b
	Model 3 [β (SE)]	Model 3 [β (SE)]	Model 3 [β (SE)]
Pain measure listed in column	-0.001 (0.0009)	-0.007 (0.017)	-0.061 (0.022)**
Depressive symptoms	-0.006 (0.002)*	-0.006 (0.002)**	-0.005 (0.002)*
Age (years)	-0.008 (0.007)	-0.009 (0.007)	-0.007 (0.007)
Race/ethnicity ^c			
African American	-0.397 (0.046)***	-0.399 (0.046)***	-0.390 (0.046)***
Chinese	-0.150 (0.082)	-0.148 (0.083)	-0.131 (0.082)
Japanese	-0.127 (0.075)	-0.125 (0.075)	-0.129 (0.074)
Socioeconomic variables			
Economic hardship	-0.098 (0.035)**	-0.102 (0.035)**	-0.089 (0.035)*
Education level	0.120 (0.016)***	0.120 (0.016)***	0.122 (0.016)***
Study site ^d			
Michigan	-0.093 (0.074)	-0.098 (0.074)	-0.089 (0.074)
Boston	-0.193 (0.071)**	-0.190 (0.071)**	-0.202 (0.071)**
Chicago	-0.058 (0.078)	-0.056 (0.079)	-0.063 (0.078)
Davis	-0.023 (0.082)	-0.026 (0.083)	-0.025 (0.082)
Pittsburgh	0.046 (0.071)	0.048 (0.071)	0.042 (0.071)
Menopausal transition stage ^e			
Premenopausal	0.299 (0.136)*	0.297 (0.135)*	0.304 (0.135)*
Post menopausal	0.006 (0.041)	0.006 (0.041)	0.008 (0.041)
Surgically postmenopausal	-0.102 (0.074)	-0.105 (0.074)	-0.098 (0.074)
Status undeterminable ^f	-0.027 (0.085)	-0.030 (0.085)	-0.024 (0.085)
Pain medications ^g			
Opioid-based pain medication ^h	-0.211 (0.127)	-0.242 (0.125)	-0.178 (0.128)
Non-opioid-based pain medication ^h	-0.021 (0.044)	-0.031 (0.044)	-0.013 (0.043)

^a*P value<0.05 **P value <0.01 ***P value <0.001

^bA higher score is interpreted as more pain

^cThe reference group for race/ethnicity is non-Hispanic white

^dThe reference group for site is the Los Angeles study site

^eThe reference group for menopausal transition stage is peri-menopause

^f“Status undeterminable” consisted of pre- and perimenopausal women using hormones

^gThe reference group for pain medication is had not taken prescription or over-the-counter pain medication at least 2 times per week in past month

^hTook medication at least 2 times per week in past month