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Severe Pain Confounds Neuropsychological Test Performance*

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Abstract

There is little information on the effect of pain on neuropsychological test performance. We have undertaken this study to explore which tests are affected by pain, the magnitude of these changes, and other confounders of neuropsychological performance in a population of patients having spine surgery. Twenty-four elderly English speaking Caucasian patients (age > 60 years) were enrolled pre-operatively in this Institutional Review Board approved study. Pain scores using an 11-point Numeric Pain Intensity scale and performance on a neuropsychological battery (Controlled Oral Word Association, Rey Complex Figure, Trails A and B) were assessed at two times, before and one day after surgery. Scores were calculated using the standard algorithms and change scores were calculated by subtracting the baseline from follow-up scores. After surgery, performance on the Rey Complex Figure ($r = -0.577, p = 0.004$) and Trails Part A ($r = 0.527, p = 0.01$) declined with increasing post-operative pain scores. Women reported higher pain scores post-operatively than men ($p = 0.046$), and performed worse than men for change in performance on Trails Part A ($p = 0.027$). These data suggest that pain can influence performance on certain cognitive tests, and that some gender differences in these effects may occur. Interpretation of performance measures should take into account possible effects of pain, although our understanding of pain effects and ability to predict them in individual people, currently are quite limited.

Neuropsychological testing is an important tool to assess effects of brain disorders on cognitive performance. However, a number of potentially confounding factors also can interfere with performance. Among these can be pain. For example, pain has been shown to interfere with attentional mechanisms (Eccleston & Crombez, 1999) as well as with memory and concentration (Grace, Nielson, Hopkins, & Berg, 1999). We often use neuropsychological testing to evaluate outcome after surgery. In some surgeries pain is not a significant factor, for example in coronary artery bypass graft surgery or carotid endarterectomy. However, in other surgeries such as spine surgery, pain is present both before and after surgery. Therefore, pain may interfere with cognitive test performance. This study was undertaken to evaluate the effect of pain on cognitive performance after spine surgery.

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METHOD

Participants

Patient information is detailed in Table 1.

Twenty-four patients (70.8% male, 29.2% female) undergoing elective lumbar spine surgery were recruited to participate in this Institutional Review Board approved study. Age ranged from 61 to 86 years ($M = 73.9$, $SD = 6.7$). Level of education ranged from 12 to 20 years ($M = 15.8$, $SD = 2.7$). All patients were Caucasian, native English speakers. Written informed consent was obtained from each patient. One patient was eliminated from the analysis because he was unable to tolerate the upright position required to perform the tests. Three patients suffered from a previous stroke or transient ischemic attack and two patients underwent carotid endarterectomy. In addition, five patients had suffered myocardial infarction in the past. No other patients had a history of pre-operative cerebral damage. No patients had any history of alcohol or other substance abuse.

Anesthesia and Surgery

All patients received general endotracheal anesthesia and continuous hemodynamic and temperature monitoring. Anesthetic agents included fentanyl ($M = 2.5$ $\mu\text{g/kg}$, $SD = 1.2$ $\mu\text{g/kg}$) and midazolam ($M = 0.03$ $\mu\text{g/kg}$, $SD = 0.02$ $\mu\text{g/kg}$). Each patient was placed in the prone position and underwent a midline incision for lumbar spine surgery (12% discectomy, 88% laminectomy). Surgical time averaged 130.4 minutes ($SD = 37.8$). All patients were extubated in the operating room and recovered for 1-3 hours in a post-operative care unit. None required a stay in the intensive care unit. All patients remained in the hospital for post-operative pain scoring and neuropsychological testing.

Measures

Patients were assessed with a battery of neuropsychological tests pre-operatively and one day post-operatively either in a quiet office or in their private hospital room. All examinations were administered by the same research assistant (R.S.), trained to administer and score these neuropsychological tests under the supervision of neuropsychologists (R.M.L., Y.S.). Three neuropsychological tests, which were chosen to represent a range of cognitive domains, were administered: Trails Parts A and B, Controlled Oral Word Association test (COWA), and the Rey Complex Figure (Lezak, 1995). For the Rey Complex Figure, a standardized scoring system (Meyers & Meyers, 1995) was used to score both the presence of specific design features and the accuracy of their location. A lower score indicated a decline in performance for all of the tests except Trails Parts A and B, where an increase in score indicated a decline in performance.

The degree of pain was measured at the same time neuropsychological testing was performed. Pain was measured using a standardized 11-point Numeric Pain Intensity Scale, with a score of zero representing no pain and a score of ten representing the worst possible pain (Fig. 1). Patients circled the number corresponding to their level of pain in the sitting position. This scale, adapted from a previous study (Downie et al., 1978), has been validated in chronic pain patients (Jensen, Karoly, & Braver, 1986) and in post-operative acute pain patients (Jensen, Karoly, O'Riordan, Bland, & Burns, 1989; Seymour, 1982).

Pre-operative depression and use of pain medication before and after surgery was determined by chart review, which included a standardized pre-operative patient questionnaire. Twenty-one out of twenty-three charts were reviewed in this manner. Two patients were on antidepressant medication at the same dosages pre- and post-operatively. No patients were on analgesic medications with central nervous system (CNS) effects pre-operatively, however ten

patients were on analgesic medications with CNS effects post-operatively, including Percocet, (oxycodone and acetaminophen; 14%), morphine (14%), and both Percocet and morphine (19%). Analgesic medications without CNS effects such as aspirin, acetaminophen (Tylenol), and ketorolac tromethamine (Toradol) were also administered post-operatively. Only one patient had a dose of morphine administered within three hours of his post-operative testing. No patients had Percocet near the time of post-operative testing.

RESULTS

Intraoperative variables such as duration of surgery and amount of anesthetic used were analyzed and were found to be unrelated to change in neuropsychological test performance.

Relationship Between Pain Scores and Test Performance

Pre-and post-operative test performance, and their means and standard deviations are shown for all of the patients in Table 2.

Two-tailed bivariate Pearson correlations were performed between pre-operative pain (Pain 1) and test scores at baseline (Tests 1), and post-operative pain (Pain 2) and test scores after surgery (Tests 2). The change in pain (Pain 2 minus Pain 1) and the changes in test scores (Tests 2 minus Tests 1) were also compared using two-tailed bivariate correlations. While Pain 1 was not correlated with any pre-operative neuropsychological test, Pain 2 was correlated with post-operative performance on both Rey Complex Figure ($r = -0.577, p = 0.004$) and Trails A ($r = 0.527, p = 0.01$; see Fig. 2). The change in pain (Pain 2 minus Pain 1) was not correlated with the change in test scores (Tests 2 minus Tests 1). However, pre- and post-operative pain levels were correlated with each other ($r = 0.538, p = 0.008$).

Women reported significantly more pain after surgery than men ($t = 2.12, p = 0.046$). Patients taking either Percocet or morphine post-operatively performed worse than those not taking these medications when change in performance scores for COWA (Percocet; $p = 0.046$) or Rey Complex Figure (morphine; $p = 0.011$) was analyzed.

DISCUSSION

We measured post-operative pain levels using a standardized 11-point Numeric Pain Intensity Scale. This pain scoring system has been studied extensively in a variety of chronic and acute pain populations (Jensen et al., 1986; Jensen et al., 1989; Seymour, 1982). Furthermore, it has proven reliable and easy to administer.

To demonstrate pure effects of pain on neuropsychological testing, ideally there would be a pain-free time during which the patients could undergo testing to establish a performance baseline. This was impossible with patients having lumbar spine surgery because almost all of these patients had pain at baseline. Our goal was to see if there was a correlation between pain before and after surgery with neuropsychological test performance. Therefore, we assessed performance on each test at each time point and treated them as independent events. We appreciate that the cause and nature of the pain was probably different before and after surgery. Before surgery, patients had chronic pain most probably from nerve root irritation. After surgery this chronic pain was presumably decreased or eliminated but replaced with acute pain from the surgical trauma. While these correlations are not proof of cause and effect, nevertheless they provide evidence of the influence of pain on cognitive performance for at least some people.

Pain is subjective. It is experienced differently in each patient. While patients described different intensities of pain before and after surgery, in our study there was a strong correlation

between pre- and post-operative pain. A possible explanation is that some patients consistently report more pain. There are probably different types of pain. Pre-operative pain appears to be of a more chronic nature, while post-operative pain has a greater acute component. Previous studies have reported that chronic pain decreases performance in tests that require attention (Eccleston, Crombez, Aldrich, & Stannard, 1997). However, in our study pre-operative pain scores did not correlate with pre-operative test performance suggesting that chronic pain may have less influence on neuropsychological performance than acute pain.

Two prior studies have shown that women experience pain differently than men (Ellermeier & Westphal, 1995; Paulson, Minoshima, Morrow, & Casey, 1998). These studies, comparing females and males, have associated the reporting of greater pain by female participants at higher levels of stimulation with greater pupillary dilatation, as a marker for autonomic nervous system activity (Ellermeier & Westphal, 1995), and with cerebral perfusion changes, as a marker of increased neuronal activity (Paulson et al., 1998). Perhaps these gender dependent responses to pain account for our observation that women report more post-operative pain than men, as well as display worse post-operative Trails A performance. However, it should be acknowledged that these findings may have occurred on the basis of chance. The number of women in our sample is small ($n = 7$) and they evidenced a change in performance on only one of four tests. Further research is needed to clarify possible gender differences in the degree to which pain is likely to influence cognitive performance.

Two neuropsychological tests were affected by pain (Rey Complex Figure and Trails Part A). Previous studies have shown an effect of pain on attentional mechanisms (Eccleston et al., 1997). Our results are consistent with these in that attention dependent tasks like these tests are impaired with increasing pain. However, other tasks that also may have a strong attention component, in addition to other components, such as Trails Part B were not significantly affected. While we have no definitive explanation for this observation, it may be that Trails Part B requires other more dominant cognitive skills such as conceptional tracking that lessen the contribution of attention in determining performance.

Acute post-operative pain may also interfere with a study participant's physical ability, affecting those tests in which rapid physical manipulation is required. Indeed both Trails Part A and B, and Rey Complex Figure tests have motor components in addition to their cognitive requirements, although it might be questioned how pain in the lower spine affects tests involving movement in the upper extremities.

Analgesic medication may interfere with attention. However, in a previous study only at the very highest doses (0.3 - 0.5 mg/kg) was oral morphine shown to impair episodic retrieval, and not motor, perceptual, or attentional tasks (Cleeland et al., 1996). Because of the danger of drawing conclusions when using multiple statistical comparisons, the association of Percocet with COWA, and morphine with the Rey Complex Figure may be problematic. In fact, none of our patients were on doses felt to interfere with cognitive testing.

How can we correct for the effect of pain on neuropsychological test performance? The present data suggest that pre-operative and post-operative pain may differently affect neuropsychological test performance. At a minimum, the levels of pain should be recorded and, if possible, effects on performance should be considered in interpretation of clinical assessments. In future research it may be possible to determine a threshold pain score above which we are uncertain of the accuracy of the assessment of neuropsychological performance. For example, using a graph of pain versus performance (Fig. 2) one can see that pain > 5 increases the time to perform Trails Part A.

However, clear-cut pain thresholds can not be as easily determined for all tests and there is likely to be considerable variability among individuals in the degree to which pain can be

tolerated without affecting performance. Additional research is needed to clarify characteristics of people and of pain that are likely to be important determinants of these effects.

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Fig. 1.
Standardized 11-point Box Scale. Patients circle the number corresponding to their level of pain at the time of the exam. A score of 0 represents no pain; a score of 10 represents the worst pain imaginable.

Fig. 2.

Scatter plot and regression line of post-operative pain and performance on Trails Part A. Higher scores indicate worse performance and more pain. A score of 0 represents no pain; a score of 10 represents the worst pain imaginable.

Table 1

Patient Information

Age, years	73.9		(6.7)
Sex (male/female)		70.8%/29.2%	
Handedness (right/left)		95.8%/4.2%	
Height, cm	174.2		(12.0)
Weight, kg	83.5		(18.8)
Education, years	15.8		(2.7)
Hypertension		62.5%	
Diabetes mellitus		12.5%	
Previous stroke or TIA		12.5%	
Previous MI		25.0%	
Previous CEA		8.3%	
Duration of surgery, min	130.4		(37.8)

Note. All values are mean (standard deviation) or percentage. TIA = Transient Ischemic Attack. MI = Myocardial Infarction; CEA = Carotid Endarterectomy.

Table 2

Test Scores

Patient #	Preoperative Test				Postoperative Test					
	Pain	COWA	Rey Figure	Trails A	Trails B	Pain	COWA	Rey Figure	Trails A	Trails B
1	0	30	36	34	89	0	27	36	32	95
2	0	48	32	50	154	0	41	33	35	149
3	6	41	24	34	59	4	40	28.5	43	76
4	4	53	31	34	64	6	34	29	35	102
5	8	36	34	26	78	4	43	33	33	52
6	2	7	33	51	138	6	14	36	57	120
7	8	39	24	54	91	5	32	12.5	48	154
8	3	64	36	61	72	1	53	34	38	87
9	0	35	28	36	71	0	43	34	43	82
10	10	39	17.5	77	300	10	42	12.5	90	284
11	2	43	21	34	65	8	49	25	30	79
12	6	33	35	45	61	3	35	34	46	86
13	4	27	33	41	58	9	38	31	62	68
14	6	35	33	38	101	4	23	31	38	98
15	2	51	33	51	98	1	51	35	55	103
16	5	30	29	44	82	4	38	26	36	80
17	3	49	27.5	34	137	8	47	26.5	45	94
18	3	42	33	49	100	0	44	33	37	91
19	2	22	31.5	45	97	2	37	25	57	90
20	1	50	30	46	178	2	46	33	28	150
21	6	39	29	39	*	3	39	32	27	*
22	3	38	23	41	98	5	42	32	47	91
23	9	50	25.5	64	143	7	39	25	77	163
Mean	4.04	39.17	29.52	44.70	106.09	4.00	39.00	29.43	45.17	108.82
Median	3.00	39.00	31.00	44.00	94.00	4.00	40.00	32.00	43.00	92.50
SD	2.92	11.90	5.00	11.68	54.77	3.05	8.93	6.41	15.58	48.85