Does cognitive function decline during the menopausal transition?

Yes But appropriately timed hormone therapy (HT) may prevent this decline. That is one of the findings of the Study of Women's Health Across the Nation (SWAN), a prospective cohort study of more than 2,300 women. SWAN also found that women who used HT *before* the final menstrual period exhibited higher cognitive functioning during perimenopause and menopause—whereas women who initiated HT *after* their last menstrual period experienced a decline in cognitive function.

Greendale GA, Huang M-H, Wight RG, et al. Effects of the menopause transition and hormone use on cognitive performance in midlife women. Neurology. 2009;72:1850–1857.

EXPERT COMMENTARY

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Dr. Kaunitz reports that he has received clinical trial support (with funding to the University of Florida Research Foundation) from Bayer, Johnson & Johnson (Ortho), Medical Diagnostic Laboratories, Schering Plough (Organon), Procter & Gamble, and Teva (Barr). He serves as a speaker or consultant for Bayer, Johnson & Johnson (Ortho), Merck, Schering Plough (Organon), Procter & Gamble, and Teva (Barr) and holds stock in Becton Dickinson and Sanofi-Aventis.

These important findings from SWAN confirm the memory problems reported by many women during the menopausal transition. They also build on the findings of clinical trials of HT in younger menopausal women, which explored the effect of HT on cardiovascular health, to underscore the critical role that timing of such therapy can play.[1,2]

Other cohort studies of middle-aged women in the United States have found the menopausal transition to be associated with undesirable changes in mood[3,4]; some experts have described the endocrine shifts that accompany menopause as "hormonal chaos."[5]

Details of the study

Participants were 42 to 52 years old and had an intact uterus and at least one ovary at entry. They were followed for 4 years, with delineation of the menopausal stage (i.e., premenopause, early and late perimenopause, and menopause) and assessment of hormone use prior to the final menstrual period and after menopause. The outcome was longitudinal performance in three cognitive domains:

- **processing speed**—assessed using the Symbol Digit Modalities Test. Premenopausal, early perimenopausal, and postmenopausal women improved with repeated administration of this test, but late perimenopausal women did not. Prior use of HT improved the score, whereas late use of HT reduced it.
- **verbal memory**—evaluated via the East Boston Memory Test. Test scores increased during premenopause and postmenopause but not during early or late perimenopause. Prior use of HT improved the test score, but late use reduced the score.

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WHAT THIS EVIDENCE MEANS FOR PRACTICE

Because perimenopausal HT should include a dosage of progestin adequate to suppress ovulation in order to prevent iatrogenic irregular uterine bleeding, women who are healthy, lean, nonsmoking, and still having menstrual periods can safely use a conventional oral contraceptive. Options for other symptomatic perimenopausal women include a continuous oral menopausal regimen formulated with 5 µg of ethinyl estradiol and 1 mg of norethindrone acetate (Femhrt 1/5) or 1 mg of estradiol and 0.5 mg of norethindrone acetate (Activella 1/0.5 or generic).

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FAST TRACK

Cognitive function declined during perimenopause, but appropriately timed hormone therapy prevented this reduction in function

- **working memory**—assessed using the Digit Span Backward test. This domain did not vary by stage of menopause.

Participants who initiated menopausal HT or oral contraceptives prior to the last menstrual period were excluded from the analysis during use of HT. They were allowed to reenter the study, however, once HT or oral contraceptives were discontinued.

As the cognitive component of SWAN began, the mean age of participants was 50 years, and 8% were premenopausal, 49% were early perimenopausal, 12% were late perimenopausal, and 27% were postmenopausal. In addition, 4% were both postmenopausal and current users of HT.

References

1. Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA. 2007;297:1465–1477.
2. Manson JE, Allison MA, Rossouw JE, et al, for the WHI and WHI-CACS Investigators. Estrogen therapy and coronary-artery calcification. N Engl J Med. 2007;356:2591–2602.
3. Freeman EW, Sammel MD, Lin H, et al. Symptoms associated with the menopausal transition and reproductive hormones in midlife women. Obstet Gynecol. 2007;110(2 Pt 1):230–240.
4. Woods NF, Smith-DiJulio K, Percival DB, Tao EY, Mariella A, Mitchell S. Depressed mood during the menopausal transition and early postmenopause: observations from the Seattle Midlife Women's Health Study. Menopause. 2008;15:223–232.
5. Berga SL. Disordered folliculogenesis during the menopausal transition: explaining chaos. Menopause. 2009;16:11–12.

Are staples or sutures better for closing the skin at cesarean delivery?

Staples are better

FAST TRACK

Use of staples for skin closure during cesarean delivery produced less pain, shorter operative time, and cosmesis comparable to sutures

—at least according to this randomized, controlled trial of 101 women. Skin closure using staples produced significantly less pain 6 weeks postoperatively, shorter operative time, and cosmesis comparable to sutures. Women were equally satisfied with the outcome, regardless of whether staples or sutures were used.

Rousseau JA, Girard K, Turcot-Lemay L, Thomas N. A randomized study comparing skin closure in cesarean sections: staples vs subcuticular sutures. Am J Obstet Gynecol. 2009;200:265.e1–265.e4.

EXPERT COMMENTARY

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The rate of cesarean delivery in the United States reached its highest level yet—31.8%—in 2007.[1] At more than 1.2 million procedures each year, cesarean delivery is the most common major surgery performed, but few studies have explored the techniques involved. Recent investigations have focused on whether it is advisable to close the peritoneum at the time of cesarean section,[2] how to perform and close the hysterotomy,[3] and the timing of prophylactic antibiotics.[4,5] But we need more evidence to optimize outcomes.

Rousseau and colleagues have made a commendable effort to sift through one of the many unanswered questions regarding cesarean technique: What is the best skin closure? Their prospective, randomized, controlled trial compared staple closure with subcuticular closure using 4-0 Monocryl.

The authors did many things we have come to expect from clinical trials, including:

- a priori sample-size calculation to ensure adequate statistical power
- randomization by group of 8
- stratification of randomization by primary and repeat cesarean delivery
- assessment of wound cosmesis in a blinded, masked fashion.

They found a "statistically significant" difference in the pain score at 6 postoperative weeks between staples and sutures, with staples having the lower mean score (0.2 vs 0.5; $P = .04$). They also demonstrated shorter operative time for staple closure (32 vs 41 minutes; $P < .001$).

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When such a study is published, it is easy to assume that the issue has been settled and to change or not change practice, depending on your existing technique—but that is often unwise. Every study has limitations. Even when statistically significant benefits are demonstrated, as they are in this study, it may not always be clear whether your patients match the patients in the study, or whether your technique matches what has been administered during the investigation.

In this case, a few problems need to be pointed out:

- Although the evaluation of cosmesis was by masked clinicians, assessment of the primary outcome—pain—was conducted by the patients themselves, who were not masked. One can easily see that awareness of a suture retained beneath the skin might bias a patient's perception of pain and discomfort. It would be relatively easy to mask the type of closure—even from patients—on postoperative day 1, but masking would become much more difficult when the staples needed to be removed.
- The issue of statistical analysis can sometimes be dull, but is occasionally paramount in determining validity of a study. In this case, the primary outcome—the pain scale—was considered a continuous outcome and compared using a Student's *t*-test. An important assumption in this test is that the data are normally distributed. However, the authors do not make it clear whether they tested the data for normalcy. Particularly at the 6-week evaluation, when the mean value was between 0 and 1 for both groups, it seems unlikely that the data were normally distributed. As a result, the difference in pain scores—0.2 vs 0.5—could have been driven by a few high values in one group. Statistically, this would have been easy to manage by changing the comparison to a Wilcoxon rank-sum test.

Despite these limitations, it does seem unlikely that the pain at 6 weeks would have been worse in the staple group.

These findings contrast those of another study of the same topic, which found less pain in the subcuticular suture group.[6] In that unmasked study, subcuticular closure was determined to be more "cosmetically attractive" by the patients and their physicians. Again, one needs to be concerned about bias.

FAST TRACK

Evidence is insufficient to systematically recommend one type of skin closure over another

References

1. Hamilton BE, Martin JA, Ventura SJ. Birth: Preliminary data for 2007. Natl Vital Stat Rep. 2009;57:1–23.
2. Lyell DJ, Caughey AB, Chu E, Daniels K. Peritoneal closure at primary cesarean delivery and adhesions. Obstet Gynecol. 2005;106:275–280.
3. Dodd JM, Anderson ER, Gates S. Surgical techniques for uterine incision and uterine closure at the time of caesarean section. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD004732.
4. Sullivan SA, Smith T, Chang E, Hulsey T, Vandorsten JP, Soper D. Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing postcesarean infectious morbidity: a randomized, controlled trial. Am J Obstet Gynecol. 2007;196;455.e1–455.e5.
5. Kaimal AJ, Zlatnik MG, Cheng YW, et al. Effect of change in policy regarding the timing of prophylactic antibiotics on the rate of postcesarean delivery surgical-site infections. Am J Obstet Gynecol. 2008;199:310.e1–310.e5.
6. Frishman GN, Schwartz T, Hogan JW. Closure of Pfannenstiel skin incisions. Staples vs. subcuticular suture. J Reprod Med. 1997;42(10):627–630.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

To echo the latest Cochrane review of this topic, there is insufficient evidence—even after this investigation—to systematically recommend one type of skin closure over another. However, given the masked evaluation of the wounds and the clear lack of difference in their appearance in this study, *cosmesis alone does not seem to be sufficient reason to utilize subcuticular sutures to close the skin at cesarean delivery. In fact, the shorter operative time documented in the staple-closure group in this study could tip the scale in favor of using staples for this procedure.*

Clearly, we need many more investigations of surgical technique and perioperative care in regard to cesarean delivery. Although I hope that cesarean section does not remain the most common surgical procedure, it seems likely that it will always be a large part of obstetric care. Therefore, optimization of outcomes merits attention.

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