

## OBSTETRICS

# Neurocognitive functioning following preeclampsia and eclampsia: a long-term follow-up study

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**OBJECTIVE:** Women who suffered preeclampsia and eclampsia may report subjective cognitive difficulties in daily life, the interpretation of which is cumbersome, because these are affected by emotional factors. Previous studies only included preeclamptic women investigated shortly after pregnancy. We aimed to determine whether these subjective reports of cognitive difficulty could be interpreted as reflecting objective cognitive dysfunction. Therefore, cognitive functioning was assessed using standardized neurocognitive tests in both preeclamptic and eclamptic women several years following the index pregnancy.

**STUDY DESIGN:** Forty-six formerly eclamptic, 51 formerly preeclamptic, and 48 control women who had normotensive pregnancies, age-matched, participated in this study. Average elapsed time since index pregnancy was 7 years. Neurocognitive tests were divided into 6 domains; visual perception, motor functions, working memory, long-term memory, attention, and executive functioning. Subjective cognitive functioning was measured by the Cognitive Failures Questionnaire and anxiety/depression by the Hospital Anxiety and Depression Scale.

**RESULTS:** Both preeclamptic and eclamptic women performed worse on the motor functions domain ( $P < .05$ ), without differences on the other domains. They scored worse on the Cognitive Failures Questionnaire ( $P < .01$ ), the Hospital Anxiety and Depression Scale anxiety ( $P < .01$ ), and depression ( $P < .05$ ) subscales.

**CONCLUSION:** Women who suffered eclampsia and/or preeclampsia demonstrate no objective cognitive impairment as compared with controls. Contrary to the well-structured test setting, both groups do report more cognitive failures, which are thought to reflect neurocognitive dysfunction in complex, stressful daily-life situations. Such report of cognitive failures may be compounded by anxiety and depression. Future studies should focus on the relationship of neurocognitive functioning with structural cerebral abnormalities.

**Key words:** anxiety and depression, cognitive complaints, eclampsia, neurocognitive functioning, preeclampsia

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Women who suffered preeclampsia and/or eclampsia report cognitive problems years after the index pregnancy.<sup>1,2</sup> Although the actual prevalence of subjective cognitive difficulties is unknown, they appear to be related to memory, concentration, and vision-related tasks of everyday life.<sup>1-4</sup>

In general, the validity of such subjective reports of cognitive functioning remains controversial, because they are also strongly influenced by noncognitive factors such as symptoms of anxiety and depression.<sup>5,6</sup> Preeclamptic women may exhibit such psychopathology after the

experience of a complicated pregnancy.<sup>7-9</sup> Alternatively, women who suffered (pre) eclampsia may have structural brain abnormalities, such as white matter lesions, potentially causing neurocognitive dysfunction.<sup>10-14</sup>

Two small studies evaluated neurocognitive test performance in preeclamptic (but not eclamptic) women within 1.5 years after the index pregnancy and found impairment on some, but not on all cognitive tests.<sup>8,15</sup> Another small study found no evidence for impaired executive functioning and sustained attention.<sup>16</sup>

Because longer follow-up of neurocognitive performance is lacking, we aimed to study cognitive functioning in a relatively large group of women who had preeclampsia and eclampsia using standardized neurocognitive tests and relate this to self-reported cognitive dysfunction and measures of anxiety and depression. We hypothesized that eclamptic women will demonstrate worse performance compared with preeclamptic women, and that both groups would perform worse than controls. Because other studies focused on more limited subdomains of cognitive functioning, we chose to cover a broader range of neurocognitive functions including tasks associated with the posterior brain areas (eg, visual functioning tasks) as well as the frontal brain areas (eg, attention and executive functioning).

## MATERIALS AND METHODS

### Participants

All eclamptic, preeclamptic, and control women with normotensive pregnancies, who were enrolled in a previous follow-

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up study, received a new invitation.<sup>10,11</sup> Recruitment and selection criteria have been published previously.<sup>10,11,14</sup> Eclampsia and preeclampsia were defined according to international criteria.<sup>17</sup> Preeclampsia was defined as de novo hypertension after 20 weeks' gestation and properly documented proteinuria. Eclampsia was defined as new onset of seizures in women with preeclampsia. Early-onset (pre)eclampsia was defined as indicated delivery <34 weeks' gestational age. Medical records were reviewed for accurateness of diagnosis and to extract clinical and demographic characteristics. This project was approved by the University Medical Center Groningen Institutional Review Board and all women signed informed consent. Measurements were performed between November 2008 and January 2012.

Exclusion criteria were epilepsy, a known cerebrovascular accident, demyelinating disorders, intracranial infections, a history of any cranial neurosurgic procedure, the inability to understand Dutch, or pregnancy at the moment of testing. Women who indicated the presence of a mood disorder

were not excluded. For all women, elapsed time since the index pregnancy had to be at least 12 months. Of the 63 eclamptic women who participated in the previous studies,<sup>10,11,14</sup> 48 (76%) could be contacted again and were willing to participate in the present study. Of the 74 preeclamptic and 75 parous control participants participating in previous studies,<sup>10,11,14</sup> respectively, 47 (64%) and 43 (57%) could be contacted again and were willing to participate. Four preeclamptic women who delivered in other hospitals and who had heard about the study requested to participate in the current study, which was allowed. Six additional control participants were included. During the study, 2 eclamptic women were excluded as they showed signs of malingering or underachievement. This was evaluated by the Amsterdam Short-Term Memory (ASTM) test, a symptom validation test presented as a short-term memory task.<sup>18,19</sup> The ASTM test is a valid, standardized, and widely used test to indicate malingering. Excluding these women did not significantly alter the results. One control was excluded

because she had professional knowledge of the neurocognitive tasks. Forty-six eclamptic women, 51 preeclamptic women, and 48 controls remained available for analysis.

Age and level of education were similar in the 3 groups (Table 1). Education level was categorized according to the system of Verhage as described by Bouma<sup>19</sup> (1 being the lowest [less than primary school], and 7 the highest [academic degree, such as bachelor/master]). None of the women were in the low education group (category 1 or 2). Average was defined as category 3-5 and as high as category 6-7. The Dutch Adult Reading Test (DART; Dutch version of the National Adult Reading Test) was used to determine premorbid intelligence.<sup>19,20</sup> The DART is a valid, standardized test based on the assumptions that reading ability (of irregular words) is relatively independent of brain disorders, and that it is a strong predictor of intelligence in the normal population.<sup>19,20</sup> No significant difference was found between the groups. One participant had sufficient knowledge of the Dutch language to fulfil the tasks, but the

**TABLE 1**  
**Overview of participant characteristics**

Characteristic	Eclampsia (n = 46)	Preeclampsia (n = 51)	Controls (n = 48)	P value
Age, y	39 (6.5)	39 (6.7)	40 (7.3)	.56
White, n (%)	44 (96)	51 (100)	46 (96)	.40
Elapsed time since index pregnancy, y	8 (2-20)	6 (1-18)	6 (1-27)	.02
Birthweight, g	1310 (300-4440)	1960 (310-4470)	3600 (2210-4620)	< .01
EGA at delivery, wk	32 (22-42 <sup>+1</sup> )	34 <sup>+4</sup> (26 <sup>+2</sup> -41)	40 (36 <sup>+2</sup> -40 <sup>+2</sup> )	< .01
SGA <10th percentile, n (%)	14 (30)	20 (39)	4 (8)	< .01
Early-onset (pre)eclampsia <34 wk, n (%)	28 (61)	24 (47)		
Nulliparous at index pregnancy, n (%)	40 (87)	34 (67)	21 (44)	< .01
Level of education, n (%)				
Average	18 (39)	24 (47)	18 (38)	.59
High	28 (61)	27 (54)	30 (63)	
DART IQ	99 (11.1)	98 (10.7)	99 (10.5)	.87
Antidepressants, n (%)	0 (0)	6 (12)	2 (4)	.99

Results are expressed as mean (SD), median (min-max), or number (percentage).

DART, Dutch Adult Reading Test; EGA, estimated gestational age; SGA, small for gestational age.

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