

Basilar Artery Response to Hyperventilation in Panic Disorder

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Objective: The purpose of this study was to measure the response of basilar artery blood flow to hyperventilation in patients with panic disorder. **Method:** Transcranial Doppler ultrasonography was used to measure basilar artery flow during rest and after hyperventilation in 16 patients with panic disorder and eight normal comparison subjects. The subjects rated their dizziness at each phase. **Results:** The patients with panic disorder demonstrated greater reduction in flow rates and greater increases in dizziness than the normal comparison subjects. **Conclusions:** The greater basilar artery sensitivity to hyperventilation shown by panic disorder patients suggests a possible mechanism for the development of neurological symptoms during panic attacks. (Am J Psychiatry 1997; 154:1603–1604)

Panic attacks often consist of dizziness, numbness, and other symptoms that suggest transient cerebrovascular disturbance. Among possible mechanisms for the relationship between cerebral blood flow (CBF) and anxiety, the basilar artery is of particular interest as disturbances in the flow of this artery are associated with neurological symptoms (visual disturbances, light-headedness, unsteadiness) (1) that are similar to those experienced during panic attacks. The basilar artery is also the primary supply to the CNS regions implicated in panic, such as the locus ceruleus, and brain stem respiratory and autonomic centers.

Gibbs (2) reported that nine panic disorder patients in a neurology clinic experienced a significantly greater decrease in basilar artery blood flow during voluntary hyperventilation (mean decrease, 62%) than did nine normal comparison subjects (mean decrease, 36%). However, no respiratory measures were assessed during hyperventilation, and this omission is important, since changes in carbon dioxide levels are critical in regulating cerebral arterial flow (3).

The purpose of the present study was to examine the basilar artery response to hyperventilation of patients with panic disorder seen in a psychiatry clinic. After initially replicating the effect found by Gibbs, we added respiratory physiology measures to determine

whether differences in basilar artery flow could be accounted for by differences in carbon dioxide levels during hyperventilation.

METHOD

The subjects were 16 patients with panic disorder and eight normal comparison subjects. The panic patients (11 women, five men) were selected from patients in the Indiana University Anxiety Disorders Clinic who complained of dizziness or faintness as a primary symptom during attacks. Ten of the 16 patients were taking benzodiazepines or antidepressants daily but were symptomatic and seeking treatment. Six of the patients each had a secondary anxiety disorder, either generalized anxiety or social phobia.

The eight comparison subjects (five women, three men) were recruited from the clinic staff. The comparison group did not meet the criteria for any current DSM-IV axis I disorder and were matched for age (mean age for patients=41.1 years, SD=10.9; mean age for comparison subjects=38.6 years, SD=10.9).

A written informed consent statement was obtained from each subject after the procedures had been fully explained.

Basilar artery blood flow was measured by using a Neuroguard (Medasonics, Fremont, Calif.) transcranial Doppler monitoring system. In the testing of three subjects over 3 months we have found a test-retest reliability (r) of 0.85 for mean flow rate and 0.92 for peak flow rate. We also used the Novamatrix Capnograph ETCO₂ Monitor, model 1265, a capnograph that measures end-tidal carbon dioxide (pCO₂) levels.

The subjects were diagnosed with clinical interviews by either a psychiatrist (A.S.) or psychologist (S.B.) experienced in the assessment of anxiety disorders. The participants were instructed to refrain from using nicotine or caffeine for 3 hours before the transcranial Doppler examination. During the procedure, each subject was seated with his or her neck maintained in a midline, nonrotated position. The basilar artery was insonated through the foramen magnum window at a depth of 85 to 100 mm. The blood flow variables measured were mean and peak flow velocities (in centimeters per second).

After ascertainment of the basilar artery flow, measurements were taken after a 3-minute baseline, after 30 seconds of hyperventilation, and after a 3-minute recovery phase. The subjects rated their dizziness

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The authors thank Cheryl Bedwell, R.N., C.N.R.N., and Charles Cristoph, B.A., for their assistance in conducting this study.

at each phase by using a scale on which 0 represented "not at all" and 10 represented "extremely." The instructions regarding hyperventilation were to breathe as deeply and quickly as possible through the nose. For nine subjects, external nasal cannulas were placed at both nostrils to measure pCO₂ levels.

RESULTS

As a subgroup of the panic disorder patients were receiving medications, we did an initial repeated measures analysis of variance (ANOVA) on the blood flow measures and dizziness ratings with medication status as the independent variable. The patients taking medications did not differ across conditions from those without medications in peak flow ($F=0.59$, $df=1, 14$, n.s.), mean flow ($F=0.49$, $df=1, 14$, n.s.), or dizziness rating ($F=0.93$, $df=1, 13$, n.s.); therefore, further analyses were made without regard to medication status.

At rest, the panic disorder and comparison groups did not differ significantly in peak flow (panic: mean=58.8 cm/sec, $SD=15.0$; comparison: mean=53.8, $SD=14.6$) or in mean flow (panic: mean=38.8 cm/sec, $SD=10.7$; comparison: mean=37.3, $SD=9.8$). However, the panic patients were significantly more dizzy (mean rating=2.81, $SD=2.66$) than the comparison group (mean=0.00, $SD=0.00$) ($t=-4.22$, $df=21$, $p<0.01$). The dizziness rating at baseline was not associated with either peak flow ($r=0.03$, $N=24$) or mean flow ($r=-0.05$, $N=24$).

Mean flow, peak flow, and the dizziness ratings were each analyzed by a repeated measures ANOVA with diagnosis as the between-group variable. For peak blood flow, the patients with panic disorder showed a 45% decrease after hyperventilation (mean change=-26.8 cm/sec, $SD=9.4$), which was significantly greater than the 33% reduction for the comparison group (mean change=-17.8 cm/sec, $SD=6.5$) (diagnosis-by-time interaction: $F=5.39$, $df=2, 44$, $p<0.01$). For mean blood flow, the panic patients had a 55% reduction (mean change=-21.1 cm/sec, $SD=7.1$), which was significantly greater than the 42% reduction for the comparison group (mean change=-15.8 cm/sec, $SD=5.4$) (diagnosis-by-time interaction: $F=4.12$, $df=2, 44$, $p<0.05$). Similarly, the patients with panic disorder reported more dizziness after hyperventilation (mean change=3.59, $SD=1.76$) than did the comparison subjects (mean change=1.50, $SD=0.93$) (diagnosis-by-time interaction: $F=7.77$, $df=2, 42$, $p<0.01$). The increases in the dizziness ratings were associated with the percentages of the decreases in both peak flow ($r=-0.60$, $N=24$, $p<0.01$) and mean flow ($r=-0.57$, $N=24$, $p<0.01$).

In the recovery phase, both groups returned to their baseline levels of blood flow with no significant differences; however, the patients with panic disorder continued to report more dizziness (mean score=2.76, $SD=2.50$) than the comparison subjects (mean=0.00, $SD=0.00$) ($t=-3.10$, $df=21$, $p<0.01$).

For the five panic disorder patients and four comparison subjects for whom respiratory measures were obtained, we examined changes in blood flow in relationship to

pCO₂ levels. The pCO₂ level of the panic disorder patients decreased 33% during hyperventilation (pCO₂ level during hyperventilation: mean=24.80 mm Hg, $SD=7.29$), which did not differ significantly from the 37% decrease for the comparison subjects (pCO₂ during hyperventilation: mean=24.55 mm Hg, $SD=3.09$) ($t=-0.14$, $df=7$, n.s.). We calculated a ratio index by dividing the decrease in percentage of mean blood flow change by the percentage decrease in pCO₂. For the panic patients the mean ratio was 2.02 ($SD=1.64$), whereas for the comparison subjects the mean ratio was 1.17 ($SD=0.34$) ($t=-1.00$, $df=7$, n.s.). The mean ratio index for the peak flow measures was 1.57 ($SD=1.26$) for the panic patients and 0.96 ($SD=0.30$) for the comparison subjects ($t=-0.93$, $df=7$, n.s.).

DISCUSSION

The results from this preliminary study indicate that patients with panic disorder demonstrate a greater basilar artery sensitivity and a greater subjective experience of dizziness than normal comparison subjects in response to brief hyperventilation. The ratio of blood flow changes to pCO₂ changes is approximately 1.0 in normative studies (4), which is consistent with the values for our comparison group. The patients with panic disorder had a ratio of blood flow change to pCO₂ change that was almost twice that of the normal subjects. This suggests that the sensitivity of the basilar artery in patients with anxiety disorders may not be due solely to changes in respiratory physiology.

The differences in vascular sensitivity between the patients with panic disorder and the comparison group may partly explain the hypersensitivity of patients with panic disorder. In cognitive behavioral models of panic disorder, panic attacks occur as a learned emotional response to bodily symptoms that are catastrophically misinterpreted, leading to the psychological development of "fear of fear" (as described in reference 5). The greater flow changes in the basilar artery may predispose panic patients to have more awareness of these symptoms, which act as a cue for cognitive misinterpretation.

Although the present findings indicate a role for the basilar artery in panic, measurements need to be done for other intracranial arteries, such as the middle cerebral artery, to determine the specificity of these findings.

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