Disruptive Effects of Acute Hypoglycemia on Speed of Cognitive and Motor Performance

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OBJECTIVE — To directly examine whether hypoglycemia differentially slows cognitive versus motor function, to evaluate the reliability of hypoglycemic-related slowing, and to examine factors contributing to individual differences.

RESEARCH DESIGN AND METHODS — IDDM subjects (n = 10) were administered a pure cognitive and a pure motor neuropsychological test at euglycemia (5.4 mmol), blood glucose nadir (2.6 mmol), postnadir (3.6 mmol), and again at euglycemia (6.7 mmol). To assess the practice effect, matched control subjects were tested at similar time intervals.

RESULTS — Concurrent and test-retest reliability for all tests was robust (r = 0.68–0.94). Only cognitive tasks demonstrated impairment at nadir ($P < 0.04$). Individual differences, in terms of cognitive impairment, were significantly correlated with levels of blood glucose at nadir and baseline performance.

CONCLUSIONS — Cognitive tasks appear to be more sensitive to neuroglycopenia than motor tasks. Cognitive impairment caused by hypoglycemia is reliable and differs across subjects. Individuals who show reliable sensitivity to cognitive impairments of hypoglycemia should avoid moderately low blood glucose levels.

The literature suggests acute hypoglycemia slows neuropsychological functioning (1–3). This study investigates whether hypoglycemia equally affects cognitive and motor functions. So far, only one report has used a purely cognitive and a purely motor task. Pramming et al. (3), using only male IDDM subjects, reported that although the cognitive task serial subtractions was not impaired at a blood glucose level of 2.9 mmol, it was impaired at a blood glucose level of 1.8 mmol. Their motor task, finger tapping, was not significantly affected at either blood glucose level. Data were not presented for individual subjects, but Pramming reported, "These results were not due to changes in individual subjects alone, but were consistent for the whole group" (3).

By directly comparing a pure cognitive task with a pure motor task, we investigated the following questions: *1*) Would hypoglycemic-induced performance slowing be similar for a cognitive task compared with a motor task? 2) Would performance across similar cognitive and similar motor tasks be reliable? 3) Would performance decrements return to the baseline function when euglycemia was re-established? and 4) What accounts for any individual differences in hypoglycemia-related deficits?

RESEARCH DESIGN AND METHODS

— As a pilot study, we took advantage of an ongoing project assessing counterregulatory integrity that used a standard insulin infusion protocol to induce hypoglycemia (5). The subjects were 10 IDDM patients (4 males), with a mean age of 34 yr, a mean GHb of 9.8%, a mean diabetes duration of 18 yr, and educational levels ranging from high school graduate to postgraduate college education. Subjects were hospitalized and received overnight regular insulin intravenously to maintain euglycemia. All long-acting insulin had been stopped at least 48 h before testing. Testing occurred the next morning during euglycemia (mean = 5.4 mmol, Fig. 1 [*EuPre*]) at 0900, blood glucose nadir (mean = 2.6 mmol) at 1030, partial recovery from hypoglycemia at 1130 (mean = 3.6 mmol, Fig. 1 [*NaPo*]), and again at euglycemia at 1200 (mean = 6.7 mmol, Fig. 1 [*EuPo*]).

To assess pure motor function,

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IDDM, insulin-dependent diabetes mellitus; FTT, finger tapping test; PASAT, Paced Auditory Serial Addition Test; MANOVA, multiple analysis of variance.

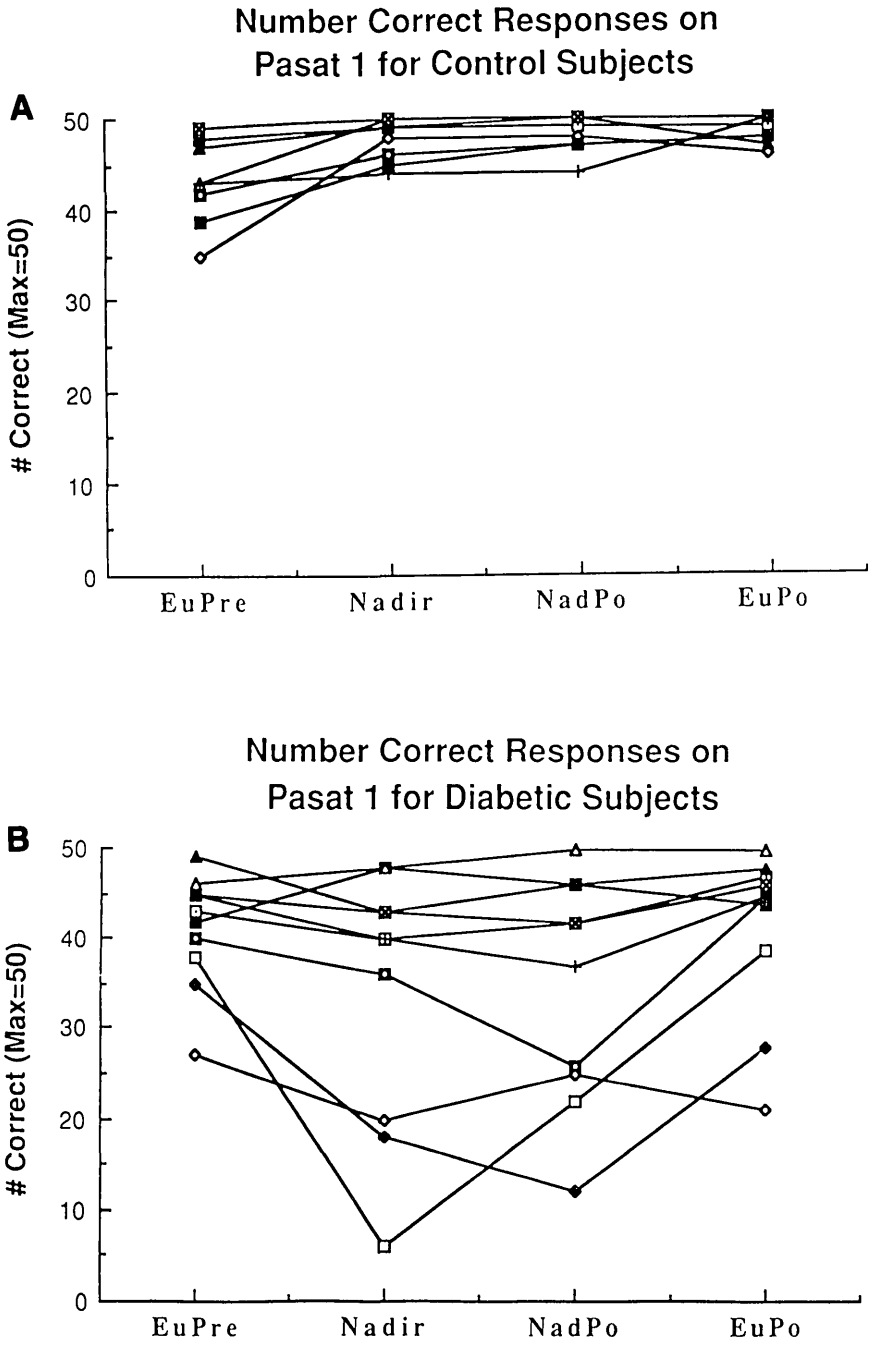

Figure 1—*Number of correct responses on PASAT 1 for control (A) and diabetic subjects (B).*

we used the FTT, which required subjects to press a telegraph-like key as rapidly as possible. To assess pure cognitive function we used the PASAT, which required subjects to listen to an audio tape and perform mental additions. To assess reliability of performance, two FTT trials and two versions of the PASAT (levels 1 and 2) were used at each of the four testings. To control for practice effects, 10 nondiabetic, healthy control subjects, who were matched on age, sex, education, and employment, were studied. Control subjects were given the same tests, in the same sequence, and at the same time intervals, but did not undergo blood glucose manipulations.

RESULTS— Performance on the two forms of similar tasks (e.g., PASAT 1 and 2) at all blood glucose levels was highly reliable, with correlation coefficients ranging from 0.72 to 0.91. Test-retest reliability of the same tasks across the two euglycemic testings (*EuPre-EuPo*) was also quite stable, with correlations ranging from 0.68 to 0.94 for the four tasks.

MANOVA analyses indicated only the cognitive tasks (PASAT levels 1 and 2) were disrupted and only at blood glucose nadir (mean = 2.6 mmol, PASAT 1 subjects versus control subjects $P < 0.04$, PASAT 2 subjects versus control subjects $P < 0.03$). As illustrated in Fig. 1, marked individual differences for the PASAT performance were observed among subjects during hypoglycemia. The percentage of decay at nadir from *PreEu* was unrelated to age, sex, education, GHb, or release of either epinephrine or pancreatic polypeptide. Performance decay was significantly related to baseline performance for PASAT 1 ($r = 0.59$), PASAT 2 ($r = 0.69$), and FTT 1 ($r = 0.65$); performance decay was also related to absolute blood glucose level at nadir for PASAT 1 ($r = 0.72$) and PASAT 2 ($r = 0.61$).

CONCLUSIONS— These data suggest that purely cognitive skills are more readily disrupted by, and thus more sensitive to, hypoglycemia than purely motor tasks. Although these tasks were not equated on level of difficulty, a recent study suggests that more difficult versions of the same tasks are not associated with greater hypoglycemic impairment (L.A.G.F., D.J.C., N. Driesen, O.M. Ryan, W.L.C., unpublished observations). The current findings were highly stable for the same tasks over time and between similar tasks at the same times. However,

subjects were not equally affected. Of the 10 subjects, 2 showed no hypoglycemic PASAT effect and only 5 subjects showed a decay in performance of >30%.

Unlike previous reports, these individual differences were not associated with sex (L.A.G.F., D.J.C., N. Driesen, O.M. Ryan, W.L.C., unpublished observations; 5) or pancreatic polypeptide release (6). This lack of replication may be caused by the use of different cognitive-motor tasks in the different studies. Two factors accounted for our individual differences on the cognitive tasks: first, the greater the hypoglycemia during nadir, the greater the decrement in performance. This finding is not surprising, because the greater the hypoglycemia, the greater the presumed neuroglycopenia. Secondly, the poorer the initial performance, the greater the performance decay during moderate hypoglycemia. This is illustrated in Fig. 1, where subjects who scored <40 on PASAT at *EuPre* showed the greatest decrement in performance.

These preliminary findings suggest that one should not assume all patients with IDDM suffer equivalent cognitive-motor deficits at moderate hypoglycemia. Future research should investigate factors that may account for such individual differences and whether these differences are stable over time within the same patients. If some individuals are consistently more sensitive to hypoglycemia, they should be strongly encouraged to avoid moderate hypoglycemia, especially at times when cognitive functioning is important.

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