Effect of diabetes on some primitive reflexes

G. Volpe\textsuperscript{a}, G. Della Rocca\textsuperscript{a}, V. Brescia Morra\textsuperscript{a}, G. Belfiore\textsuperscript{b}, G. Coppola\textsuperscript{a}, G. Campanella\textsuperscript{a} and G. Orefice\textsuperscript{a}

\textsuperscript{a}Department of Neurological Sciences, University Federico II, Naples; and \textsuperscript{b}Department of Neurology, Hospital Vito Fazzi, Lecce, Italy

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Primitive reflexes (PRs) are present in newborns; they disappear as the brain matures and increase in frequency in healthy elderly individuals. Primitive reflexes are more frequent in some neurological disorders than in age-matched controls. The aim of this study was to investigate the effect of diabetes on some PRs. We examined three PRs (glabellar tap, snout and palomental reflexes) in 376 subjects: 111 normal age-matched controls, 60 patients with cerebrovascular disease (CVD) and 205 patients with type 2 diabetes mellitus. The latter patients were divided into three groups: (1) diabetics without neurological complications (D); (2) diabetics with cerebrovascular disease (D-CVD); and (3) diabetics with polyneuropathy (D-PN). The frequency of PRs was increased in CVD, unchanged in D-CVD (except palomental) and greatly reduced in D and D-PN. It is possible that the vascular lesions in perforating arteries of the pons in diabetic subjects, previously studied in some pathological reports, can account for the reduced occurrence of primitive reflex responses.

Introduction

Primitive reflexes (PRs) such as the glabellar tap, and snout and palomental reflexes, are present in newborns. They disappear as the brain matures and increase in frequency in healthy elderly individuals (Ansink, 1962; Otomo \textit{et al}. 1965; Marti-Vilalta and Graus, 1984; Odenheimer \textit{et al}. 1994). These reflexes are believed to represent ‘release’ phenomena, probably resulting from the loss of inhibition by suprasegmentary cerebral structures (Paulson and Gottlieb, 1968). The palomental reflex is present in 25% of healthy newborns. The frequency drops to 11% in healthy adults, increases to 27% after the age of 50 and to 53.5% after the age of 60 (Demeurisse \textit{et al}. 1979; Marti-Vilalta \textit{et al}., 1984).

Primitive reflexes have been found more frequently in some neurological disorders than in age-matched controls. The frequency of one or more PRs is increased in Parkinson’s disease (Vreeling \textit{et al}. 1993), in cases of incidental cerebral lesions detected with magnetic resonance imaging (Kobayashi \textit{et al}. 1990), and in patients affected by cerebrovascular damage associated with hemiplegia (Demeurisse \textit{et al}. 1979). Isakov \textit{et al}. (1984) reported that only the combination of two or three PRs distinguished neurologically damaged patients from normal age-matched controls.

The aim of the present study was to evaluate the frequency of three PRs (glabellar tap, and snout and palomental reflexes) in patients type 2 diabetes mellitus with or without the central and peripheral nervous system complications associated with the disease.

Subjects

A total of 376 subjects (265 consecutive out-patients and 111 normal controls) entered the study. They were divided into five groups (Table 1).

Group NC consisted of healthy control subjects, living in rest homes for elderly people. These subjects were not affected by neurological or psychiatric disorders or by systemic or dysmetabolic diseases. Their neurological examination was normal (see Methods). The controls were age-matched to the patients in the other four groups. Group D consisted of subjects with a diagnosis of type 2 diabetes who did not show the neurological complications of diabetes (CVD and/or polyneuropathy) upon clinical examination. Group D-CVD consisted of patients with type 2 diabetes and with signs of a previous unilateral cerebral ischemic stroke. In all these patients diabetes was diagnosed before stroke. Group D-PN was comprised subjects with type 2 diabetes and clinical evidence of peripheral polyneuropathy. Diabetic polyneuropathy was diagnosed according to the clinical criteria proposed by...
Dyck et al. (1987), i.e. decreased vibration sense and absence of one or more deep tendon reflexes in the lower limbs. The age-matched reference values of vibration sense are reported elsewhere (De Michele et al., 1991). The subjects of the last three groups were recruited in two out-patient diabetic care units, where fasting blood glucose and HbA1 were determined at regular intervals. Group CVD consisted of out-patients with signs of a past unilateral ischemic stroke, and without clinical and laboratory evidence of diabetes. The occurrence of stroke in the D-CVD and CVD groups was verified by the examination of a previous computed tomography. The time of stroke onset ranged from three months to three years before entering the study.

All subjects gave their informed consent prior to their inclusion in the study.

Methods

All controls and patients were first submitted by a trained neurologist (GV, GDR, VBM or GB) to a standard neurological examination consisting of the following items: gait, Romberg test, cranial nerves, speech, neck and limb tonus, deep tendon reflexes, pyramidal signs, vibration sense in the four limbs, finger-to-nose and diadochokinesia tests. Then, all controls and patients were examined, at different times, by two neurologists, blind to each other’s results, to evaluate the glabellar tap, and snout and palmomental reflexes. Both investigators elicited the reflexes in the same order. Subjects were invited to stay relaxed in a sitting position. They were informed about the nature of the stimulus in order to prevent possible startle reactions that might influence their response. No information was given about the nature of the expected response. All subjects gave their oral informed consent to the study.

The glabellar tap is a rapid tapping of the glabellar region with a reflex hammer that approaches the patient from above the forehead outside the visual field. Protracted reflex blinking of either the upper or lower eyelids or both constitutes an abnormal response.

The snout reflex consists of a protrusion of the subject’s lips when a slight tap is gently but firmly applied on the middle of the upper lip with a reflex hammer. During the procedure the subject is requested to keep his/her mouth loosely closed and his/her eyes closed.

The palmomental reflex consists of a brief contraction of the mentalis muscle, resulting in a wrinkling of chin skin, when the ipsilateral tenar eminence is briskly, but not painfully, stroked by a pin from the proximal to the distal end.

The snout reflex was considered present when elicited three consecutive times; the palmomental reflex was considered present when elicited twice at an interval of about 30 s; the glabellar tap was considered present when elicited at least 10 consecutive times at a rate of twice per second. The palmomental reflex was tested on both sides, and it was considered present even if it was unilateral.

Each reflex was considered present only when confirmed by both investigators. The \( \chi^2 \) test, Fisher’s exact test and analysis of variance were used for statistical analysis. The protocol of the study was approved by the Ethics Committee of our University.

Results

There were no significant differences in diabetes duration among D, D-CVD and D-PN groups (Table 1). There was a significant difference in gender distribution among the five groups (\( \chi^2 = 74.98, P < 0.01 \)). However, a comparison of the frequency of PRs between males and females within each group showed that there were no gender-related differences.

The frequency of PRs was highest in patients with CVD (Figure 1). Frequency decreased in patients with

<table>
<thead>
<tr>
<th>Sex</th>
<th>Groups</th>
<th>M</th>
<th>F</th>
<th>Total no.</th>
<th>Age [mean ± SD (range)]</th>
<th>Diabetes duration [years ± SD (range)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>38</td>
<td>73</td>
<td>111</td>
<td>70.5 ± 10.4 (50–89)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>33</td>
<td>72</td>
<td>105</td>
<td>66.7 ± 8.7 (50–85)</td>
<td>13.4 ± 7.5 (1–33)</td>
<td></td>
</tr>
<tr>
<td>D-CVD</td>
<td>29</td>
<td>23</td>
<td>52</td>
<td>69.4 ± 7.1 (52–82)</td>
<td>13.5 ± 7.6 (3–30)</td>
<td></td>
</tr>
<tr>
<td>D-PN</td>
<td>16</td>
<td>32</td>
<td>48</td>
<td>68.2 ± 7.1 (53–82)</td>
<td>15.8 ± 7.6 (4–33)</td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td>31</td>
<td>29</td>
<td>60</td>
<td>70.4 ± 8.3 (51–85)</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

NC: normal controls; D: diabetics without neurological complications; D-CVD: diabetics with cerebrovascular disease; D-PN: diabetics with polyneuropathy; CVD: cerebrovascular disease without diabetes.
D-CVD and in normal controls, and was lowest among subjects with type 2 diabetes with and without peripheral neuropathy (D-PN and D). The snout was the reflex most frequently elicited in all groups but D-CVD; on the contrary, the palmomental was the least frequently elicited in all groups but D-CVD.

There was a significant difference in the CVD group with respect to the other four groups for all PRs, except the palmo-mental reflex versus the D-CVD group (Table 2). Moreover, a significant difference in the frequency of all PRs was found between the following groups: NC versus D and D-PN, D-CVD versus D and D-PN. Groups D-CVD and NC differed only in palmo-mental frequency. There was no difference in the frequency of any PRs between groups D and D-PN.

**Discussion**

Our data confirm that PRs are more frequent in patients with CVD than in age-matched controls (Demeurisse et al., 1979; Vreeling et al., 1993). Here we demonstrate that diabetes greatly affects the occurrence of these reflexes. In our patients with CVD plus diabetes, the expected increase of PR frequency was not observed. Indeed, there was no difference in PR frequency between normal controls and D-CVD patients. Only the palmo-mental reflex showed a slight trend towards the expected increase. In patients with diabetes with or without peripheral polyneuropathy, PRs were almost completely absent, most notably the glabellar tap and the palmo-mental reflex. Gender did not seem to affect the frequency of PR.

It is generally agreed that PRs result from the impairment of suprasegmentary cerebral structures, which physiologically inhibit neuronal structures at the brainstem level or below (Paulson et al., 1968; Tweedy et al., 1982). Primitive reflexes are polysynaptic reflexes, whose centers are probably located in the brainstem (glabellar tap and snout) or in the cervical cord and brainstem (palmo-mental). The palmo-mental reflex utilizes afferent fibers belonging to the median nerve, which is the longest and most vulnerable afferent pathway of all those used by PRs.

How may one account for the reduced frequency of

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**Table 2** Comparison of PR occurrence among the five groups: results of statistical analysis

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glabellar tap</th>
<th>Snout reflex</th>
<th>Palomental reflex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D</td>
<td>D-CVD</td>
<td>D-PN</td>
</tr>
<tr>
<td>NC</td>
<td>0.0001</td>
<td>NS</td>
<td>0.001</td>
</tr>
<tr>
<td>D</td>
<td>0.0004</td>
<td>NS</td>
<td>0.0001</td>
</tr>
<tr>
<td>D-CVD</td>
<td>0.02</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>D-PN</td>
<td>0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: not significant; NC: normal controls; D-CVD: diabetics with cerebrovascular disease; CVD: cerebrovascular disease without diabetes; D: diabetics without neurological complications; D-PN: diabetics with polyneuropathy.
PRs in diabetic patients? One possibility is that diabetic polyneuropathy affects the peripheral nerves, a condition that can become clinically overt when nerve conduction is already impaired (Jensen et al., 1991). Indeed, as early as 1957 Tweedy and Reding suggested that intact lower motor neuron function may be required for the expression of these reflexes (Jenky and Reeves, 1983).

Another possible explanation is involvement of brainstem reflex centers in diabetic patients. Peress et al. (1973), in an autopsy study of 935 diabetics and 759 non-diabetics, found a high frequency of encephalomalacia or brain infarction in the brainstem of diabetics, particularly in the pons. They reported that ‘in the diabetic group, the frequency of pontine malacia is generally three to four times higher than that for non-diabetics in every age group from 25 to 85 years. Another autopsy study confirmed that the disorder is due to a specific affection of small perforating branches of the basilar artery (Kameyama et al., 1994).

The early and severe ischemic lesions of the pons in diabetic patients, with clinical signs of cerebrovascular disease, could be the key to understanding the reduced frequency of PRs in this subject group. Since PRs are all integrated in the brainstem (Jacobs and Gossman, 1980), the occurrence of supratentorial stroke probably becomes ineffective in releasing brainstem responses. Therefore, patients with diabetes and CVD have the same frequency of PRs as normal controls. In patients with diabetes and diabetic polyneuropathy (groups D and D-PN) it is possible that an early, asymptomatic involvement of the small branches of the basilar artery may affect the brainstem centers of PRs. The decrease of PRs in these groups might have the same pathogenesis as in D-CVD patients. However, we cannot exclude that peripheral polyneuropathy plays a role in the abolition of PRs, in particular of palmo-mental reflex.

In conclusion, PRs reappear in elderly people and are particularly increased in such neurological disorders as Parkinson’s disease, progressive supranuclear palsy and cerebrovascular diseases (Demeurisse et al., 1979; Vreeling et al., 1993; Valls-Solé et al., 1997). In these patients, diencephalic lesions, which cause an abnormal striatal output, or leukoaraiosis, which causes corticospinal fiber damage (Peress et al., 1973), may suppress the physiological inhibition of brainstem reflex circuits, thus resulting in PR motor responses. However, PRs are not increased or greatly reduced in patients with diabetes, either non-complicated or complicated with cerebrovascular disease or peripheral polyneuropathy. In these patients, asymptomatic vascular lesions of brainstem, associated or not with peripheral polyneuropathy, may abolish the expected frequency of PRs due to age and supratentorial vascular lesions.

References


