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Multisensory integration in the basal ganglia

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Keywords: auditory, cat, caudate nucleus, somatosensory, substantia nigra, visual

Abstract
Sensorimotor co-ordination in mammals is achieved predominantly via the activity of the basal ganglia. To investigate the underlying multisensory information processing, we recorded the neuronal responses in the caudate nucleus (CN) and substantia nigra (SN) of anaesthetized cats to visual, auditory or somatosensory stimulation alone and also to their combinations, i.e. multisensory stimuli. The main goal of the study was to ascertain whether multisensory information provides more information to the neurons than do the individual sensory components. A majority of the investigated SN and CN multisensory units exhibited significant cross–modality interactions. The multisensory response enhancements were either additive or superadditive; multisensory response depressions were also detected. CN and SN cells with facilitatory and inhibitory interactions were found in each multisensory combination. The strengths of the multisensory interactions did not differ in the two structures. A significant inverse correlation was found between the strengths of the best unimodal responses and the magnitudes of the multisensory response enhancements, i.e. the neurons with the weakest net unimodal responses exhibited the strongest enhancement effects. The onset latencies of the responses of the integrative CN and SN neurons to the multisensory stimuli were significantly shorter than those to the unimodal stimuli. These results provide evidence that the multisensory CN and SN neurons, similarly to those in the superior colliculus and related structures, have the ability to integrate multisensory information. Multisensory integration may help in the effective processing of sensory events and the changes in the environment during motor actions controlled by the basal ganglia.

Introduction
Previous studies have demonstrated that the basal ganglia play a prominent role in sensorimotor co-ordination (Schwarz et al., 1984; Lynd-Balta & Haber, 1994; Barneoud et al., 2000). Thus, neurons sensitive to visual, auditory or somatosensory modalities have been found in both the substantia nigra (SN) and the caudate nucleus (CN), and it is of interest that high proportions of neurons with multisensory properties have been described in these neuronal populations (Poudreux & Freton, 1979; Hikosaka & Wurtz, 1983; Strecker et al., 1985; Hikosaka et al., 1989; Magarinos-Ascone et al., 1994; Chudler et al., 1995; Nagy et al., 2005b). In this context, the basal ganglia seem to belong among brain structures that can sample and evaluate a wide variety of changes in their environment, irrespective of the sensory modalities.

The parallel processing of different modality sensory information may strongly increase the probability that relevant sensory events will be detected and responded to. Accordingly, complex multisensory stimuli may possess effects or carry meanings that their individual components do not have (Meredith & Stein, 1983, 1986). The brain structures that process multisensory information and contain multisensory single cells have the possibility to integrate visual, auditory and somatosensory signals.

The basic principles of multisensory cross–modality interactions have been investigated in the superior colliculus (SC) of anaesthetized or behaving cats and monkeys (Meredith & Stein, 1983, 1986; King & Palmer, 1985; Peck, 1987; Wallace & Stein, 1996; Kadunce et al., 1997; Wallace et al., 1998; Populin & Yin, 2002) and more recently in brain slices (Skaliotra et al., 2004). Several regulatory aspects of the multisensory integration in the SC have been described, i.e. the spatial rule, the temporal rule and the formulation of the relationship between the stimulus strength and the magnitude of the interaction in the description of the inverse effectiveness rule (Meredith & Stein, 1986, 1996; Wallace & Stein, 1996; Holmes & Spence, 2005).

Although the morphological and functional connections of the basal ganglia to other multisensory areas suggest the contribution of the basal ganglia to multisensory information processing (Harting et al., 2001a, b), not too many data are available concerning the multisensory integration ability of neurons in the CN and the SN. In an intracellular investigation in the CN (Wilson et al., 1983), membrane potential changes were recorded to simultaneously presented auditory stimulation and transdermal electrical shocks. Later, through the use of an extracellular single-cell recording technique, Chudler et al. (1995) described the convergence and integration of auditory and somatosensory information in the neostriatum. In the present study, we set out to analyse whether the CN and SN neurons are able to integrate multisensory information. We therefore recorded the visual, auditory, somatosensory and multisensory responses of single-units in the CN and the SN of anaesthetized, paralysed cats and compared the effects of unimodal and multisensory stimuli on the neuronal activity.

Materials and methods
Animal preparation and surgery
This study was performed on seven adult cats of either sex weighing between 2.8 and 3.3 kg. All procedures were carried out so as to
minimize the number of the animals, and followed the European Communities Council Directive of 24 November 1986 (S6609 EEC) and the National Institutes of Health guidelines for the care and use of animals for experimental procedures. The experimental protocol was accepted by the Ethical Committee for Animal Research of Albert Szent-Györgyi Medical and Pharmaceutical Centre at the University of Szeged. The cats were initially anaesthetized with ketamine hydrochloride (30 mg/kg i.m.). The trachea and the femoral vein were cannulated and the animals were placed in a stereotactic headholder. The head of each animal was fixed to a vertical metal bar with the aid of acrylicate and the ear-bars were removed. Wound edges were treated generously with procaine hydrochloride (1%). The anaesthesia was continued with halothane (1.6–2.4% during surgery and 0.8–1.0% during recordings). The depth of anaesthesia was monitored by continuous reading of the end-tidal halothane values and by repeated checks of the electroencephalogram (EEG) and electrocardiogram. There was continuous high-amplitude, low-frequency EEG activity and we checked repeatedly whether any noxious stimulation or a forceful pressing of the forepaws could induce EEG desynchronization. The minimal alveolar anaesthetic concentrations calculated from the end-tidal halothane readings always lay in the range given by Villeneuve & Casanova (2003). The animals were immobilized with gallamine triethiodide (Flaxedyl, 20 mg/kg i.v.). A liquid containing gallamine (8 mg/kg/h), glucose (10 mg/kg/h) and dextran (50 mg/kg/h) in Ringer solution was infused at a rate of 3 mL/h. The end-tidal CO2 level and the rectal temperature were monitored continuously and kept approximately constant, at 3.8–4.2% and 37–38 °C, respectively. The skull was opened with a dental drill to allow a vertical approach to the appropriate brain structures. The dura was removed and the cortical surface was covered with a 4% solution of 38 °C agar dissolved in Ringer solution. The eye contralateral to the cortical recording was treated with phenylephrine (10%) and atropine (0.1%), and was equipped with a +2 dioptre contact lens. The ipsilateral eye was covered during visual stimulation. A subcutaneous injection of 0.2 mL 0.1% atropine was administered preoperatively.

Recording and stimulation

Electrophysiological recordings on single-units were carried out extracellularly via tungsten microelectrodes (AM System Inc. USA, 2–4 MΩ). Vertical penetrations were performed between the Horsley-Clarke co-ordinates, anterior 12–16; lateral 4–6.5; in the stereotaxic depths between 12 and 19, and anterior 3–6; lateral 4–6; in the stereotaxic depths between 4 and 7, to record CN and SN single-units, respectively. At the end of the experiments, the animals were deeply anaesthetized with sodium pentobarbital (200 mg/kg i.v.) and transcardially perfused with 4% paraformaldehyde solution. The brains were removed, cut in coronal sections of 50 μm and stained with neutral red. Electrolytic lesions marked the locations of successful electrode penetrations. The recorded sensory neurons were located in the dorsolateral aspect of the CN and in the SN pars reticulata.

For visual stimulation, light spots 1–10° in diameter (depending on the stimulus size preference of each unit) were generated by a projector device equipped with an adjustable slit-lamp diaphragm. The high-contrast (70%) visual stimuli were moved through the area centralis with a computer-controlled moving mirror system and were projected across the tangent screen (52 cm in front of the animal) in the optimal moving direction and at an optimal velocity (30–120°/s) for each unit. The duration of stimulus movement was 1 s. The white noise auditory stimuli were produced by a loudspeaker positioned on the tangent screen 52 cm in front of the animal to the back reflection of the area centralis. The sound intensity near the speaker was constant at 60 dB. The duration of the auditory stimulation was 1 s. Somatosensory stimulation was delivered with the motion of a computer-controlled pen driver, whose tip was attached to nylon fibres. The surface area of the stimulator was 1 cm². The hair was shaved at the stimulation site. The stimulator was rotated that provided a constant light mechanical stimulation (pressing) on a same 1 cm² surface of the contralateral trunk of the animal. The duration of a somatosensory stimulation was also 1 s. The computer-controlled stimuli were presented in a pseudo-random order either separately (visual or auditory or somatosensory) or simultaneously in bimodal (visual-auditory, visual-somatosensory or auditory-somatosensory) or trimodal (simultaneously visual-auditory-somatosensory) combinations. Whenever a single unit was found that was visual or auditory or somatosensory-sensitive, at least ten trials were run in each condition. The interstimulus interval was consistently 1 s.

Individual action potentials were distinguished with the help of a spike-separator system (SPS-8701, Australia). The number and temporal distribution of action potentials recorded during visual, auditory, somatosensory, bimodal or trimodal stimuli were stored as peristimulus time histograms and analysed off-line by computer. Both the prestimulus time (during which we measured the spontaneous activity of the neurons) and the peristimulus time (during which we measured the neuronal responses to different sensory and multisensory stimuli) were 1000 ms.

Data analysis

The net firing rate was calculated as the difference between the firing rates during the prestimulus (1000 ms) and the peristimulus (1000 ms) intervals. When we analysed the modalities separately, we defined the net firing rate as the response when a paired t-test indicated a significant (P < 0.05) difference between the prestimulus and the peristimulus firing rates.

A cross-modal multisensory interaction was considered to exist when the difference between the net firing rate of the most effective single modality and the bimodal or trimodal peristimulus firing rate proved to be significant by analysis of variance (ANOVA, P < 0.05; Meredith & Stein, 1983). To quantify the strengths of the facilitatory interactions, the percentage enhancements were calculated via the formula coined by Meredith & Stein (1986):

\[
\text{Percentage enhancement} = 100 \times \frac{(CM - SM_{\text{max}})}{SM_{\text{max}}}
\]

To quantify the strengths of the inhibitory interactions and enable comparisons with the percentage enhancement, we introduced the formula:

\[
\text{Percentage inhibition} = 100 \times \frac{(SM_{\text{max}} - CM)}{CM}
\]

where CM is the mean number of net impulses evoked by the bimodal stimulus and SMmax is the mean number of net impulses evoked by the most effective single-modality stimulus. For this formula, an inhibition percentage equal to 100% does not mean complete abolition of the unimodal response; thus, the inhibition percentage values derived from this formula can be higher than 100%. An inhibition percentage equal to 100% means a 50% decrease in the unimodal activity, while an inhibition percentage equal to 200% means a decrease in the unimodal activity to one-third during multisensory stimulation.

To measure the onset latency of the responses, we used a software program developed in our laboratory (Eördégh et al., 2005). This was based on a sliding-window technique. The program slid two 350 ms
windows along the frequency histogram of the responses. The first window slid through the peristimulus firing rate in 5-ms steps, and selected the 350-ms wide portion that represented the maximum frequency. Then, a second window slid in 5-ms steps, and after each step the program calculated the significance level between the spike frequency values of the two windows with the t-test. The latency of the responses was calculated from the time function of these P-values. A curve was fitted to the P-values, and the time interval between the start of the stimulation and the first point of the rising segment of the curve provided the response onset latency.

Results

The multisensory integration abilities of a total of 77 CN and 75 SN pars reticulata sensory single-neurons were analysed in detail. Similarly to earlier results from our group, the extents of the visual, auditory and somatosensory receptive fields were found to be extremely large, covering almost the whole of the physically approachable sensory field (Nagy et al., 2003, 2005a, b). To exclude the differences in multisensory integration of single-neurons related to spatial variations, we attempted to make consistent use of the same stimulation sites throughout the whole study (see Materials and methods).

Significant facilitatory and inhibitory interactions in the CN and the SN

The majority of the investigated sensory neurons in the CN (Table 1) and the SN (Table 2) were multisensory. We defined a neuron as multisensory either when it reacted to two or more different sensory modalities to a statistically significant extent, or when it reacted to only one sensory modality to a significant extent, but at least one of the ineffective modalities induced a multisensory cross-modal interaction. Thirty of the 45 multisensory CN neurons (67%) and 36 of the 56 multisensory SN neurons (64%) exhibited significant multisensory interactions. Figure 1 demonstrates recordings for a CN unit that furnished significant responses to separate visual and somatosensory stimulation and displayed a significant multisensory response enhancement, while Fig. 2 presents a CN unit that exhibited a significant multisensory response depression. This unit responded to only somatosensory stimulation to a statistically significant extent, but the ineffective auditory stimulus was able to induce a multisensory response depression. Multisensory facilitatory and inhibitory interactions in the SN are demonstrated in Figs 3 and 4. Both of these SN neurons responded to only one modality (somatosensory or visual, respectively) to a statistically significant extent, but a separately presented ineffective modality induced either a response enhancement (Fig. 3) or a response depression (Fig. 4). We analysed altogether 36 interactions between the CN units (Table 1) and 39 interactions between the SN neurons (Table 2). The large majority of the interactions in both structures were multisensory response enhancements and approximately one quarter of them were multisensory response depressions. We found significant facilitatory and inhibitory interactions in both structures in each multisensory stimulus combination tested.

Magnitude of multisensory interactions in the CN and the SN

We found slightly stronger facilitatory and inhibitory multisensory interactions in the CN than in the SN (Fig. 5). Despite this, there was no significant difference (Mann–Whitney U-test, $P = 0.15$) between the strengths of the facilitatory interactions in the CN (median = 148, $N = 26$, range 44–625%) and the SN (median = 115, $N = 28$, range 40–574%). Similarly, there was no significant difference (Mann–Whitney U-test, $P = 0.22$) between the strengths of the inhibitory interactions in the CN (median = 161, $N = 10$, range 37–688%) and the SN (median = 126, $N = 11$, range 41–391%). Comparison of the strengths of the overall inhibitory and excitatory interactions between the CN (median = 140, $N = 36$, range: 37–688%) and the SN (median 116, $N = 39$, range 40–574%) demonstrated no significant difference (Mann–Whitney U-test, $P = 0.21$).

Subadditive, additive and superadditive multisensory interactions in the CN and the SN

Stanford et al. (2005) recently introduced a different way to quantify multisensory interactions in the SC. They reported subadditive, additive and superadditive response enhancement effects as concerns the relation of multisensory discharge rates to the magnitude of the unimodal responses. The classification was a subadditive interaction when the multisensory response was shown by a $t$-test to be significantly lower than the sum of the two different unimodal responses, an additive interaction when the bimodal response was not different from the sum of the unimodal responses, and a superadditive interaction when the multisensory response was significantly higher.

Table 1. Modality distribution of sensory neurons in the caudate nucleus (CN)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Number of cells (and %)</th>
<th>Nonintegrative cells</th>
<th>Integrative cells</th>
<th>Integrative cells A</th>
<th>Integrative cells B</th>
<th>Number of interactions</th>
<th>Enhancement</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unimodal</td>
<td>32 (42)</td>
<td>32 (42)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>V</td>
<td>13 (17)</td>
<td>13 (17)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>A</td>
<td>5 (6)</td>
<td>5 (6)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>S</td>
<td>14 (19)</td>
<td>14 (19)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Multisensory</td>
<td>45 (58)</td>
<td>15 (19)</td>
<td>30 (39)</td>
<td>20 (26)</td>
<td>10 (13)</td>
<td>36 (100)</td>
<td>26 (72)</td>
<td>10 (28)</td>
</tr>
<tr>
<td>V-A</td>
<td>7 (9)</td>
<td>5 (6)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2 (6)</td>
<td>2 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>V-S</td>
<td>14 (18)</td>
<td>6 (8)</td>
<td>8 (11)</td>
<td>6 (8)</td>
<td>2 (3)</td>
<td>8 (22)</td>
<td>7 (19)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>A-S</td>
<td>7 (9)</td>
<td>1 (1)</td>
<td>6 (8)</td>
<td>5 (6)</td>
<td>1 (1)</td>
<td>6 (17)</td>
<td>4 (11)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Trimodal</td>
<td>17 (22)</td>
<td>3 (4)</td>
<td>14 (18)</td>
<td>8 (11)</td>
<td>6 (8)</td>
<td>20 (55)</td>
<td>13 (36)</td>
<td>7 (19)</td>
</tr>
<tr>
<td>Altogether</td>
<td>77 (100)</td>
<td>47 (61)</td>
<td>30 (39)</td>
<td>20 (26)</td>
<td>10 (13)</td>
<td>36 (100)</td>
<td>26 (72)</td>
<td>10 (28)</td>
</tr>
</tbody>
</table>

Integrative cells A column denotes the number of CN units that reacted to only one sensory modality to a significant extent but at least one of the ineffective modalities induced a multisensory cross-modal interaction, while Integrative cells B column demonstrates the number of caudate neurons that reacted to two or three different sensory modalities to a statistically significant extent and additionally exhibited multisensory integration. The last three columns of the table denote the numbers and the distribution of cross-modal interactions within the integrative CN multisensory neurons. V, visual; A, auditory; S, somatosensory.
than the sum of the unimodal responses. We also analysed the interactions in the CN and the SN in a similar way. Ten of the 26 facilitatory interactions found in the CN and 15 of the 28 in the SN were superadditive (t-test, \( P < 0.05 \)). However, the remaining 16 facilitatory interactions in the CN and 13 in the SN were additive (t-test, \( P > 0.05 \)). In contrast, the above-mentioned ten multisensory response depressions in the CN and 11 in the SN were consistently subadditive, the multisensory net discharge rate being significantly lower than the sum of the net unimodal responses (t-test, \( P < 0.05 \)).

**Inverse effectiveness principle in the CN and the SN**

In both the CN and the SN, we investigated the correlation between the magnitudes of the best unimodal responses and the magnitudes of the response enhancements (percentage enhancements; Meredith &

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**Table 2. Modality distribution of sensory neurons in the substantia nigra (SN)**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Number of cells (and %)</th>
<th>Nonintegrative cells</th>
<th>Integrative cells</th>
<th>Integrative cells A</th>
<th>Integrative cells B</th>
<th>Number of interactions</th>
<th>Enhancement</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unimodal</td>
<td>19 (25)</td>
<td>19 (25)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>V</td>
<td>8 (11)</td>
<td>8 (11)</td>
<td>3 (3)</td>
<td>–</td>
<td>–</td>
<td>16 (21)</td>
<td>39 (100)</td>
<td>28 (72)</td>
</tr>
<tr>
<td>A</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1 (1)</td>
<td>2 (5)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>S</td>
<td>8 (11)</td>
<td>8 (11)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Multisensory</td>
<td>56 (75)</td>
<td>20 (27)</td>
<td>36 (48)</td>
<td>20 (27)</td>
<td>16 (21)</td>
<td>39 (100)</td>
<td>28 (72)</td>
<td>11 (28)</td>
</tr>
<tr>
<td>V-A</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1 (1)</td>
<td>2 (5)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>V-S</td>
<td>25 (34)</td>
<td>9 (13)</td>
<td>16 (21)</td>
<td>12 (16)</td>
<td>2 (3)</td>
<td>4 (5)</td>
<td>16 (41)</td>
<td>11 (28)</td>
</tr>
<tr>
<td>A-S</td>
<td>6 (8)</td>
<td>4 (5)</td>
<td>2 (3)</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Trimodal</td>
<td>22 (30)</td>
<td>6 (8)</td>
<td>16 (21)</td>
<td>5 (7)</td>
<td>11 (15)</td>
<td>19 (49)</td>
<td>15 (38)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Altogether</td>
<td>75 (100)</td>
<td>39 (52)</td>
<td>36 (48)</td>
<td>20 (27)</td>
<td>16 (21)</td>
<td>39 (100)</td>
<td>28 (72)</td>
<td>11 (28)</td>
</tr>
</tbody>
</table>

Integrative cells A column denotes the number of SN units that reacted to only one sensory modality to a significant extent but at least one of the ineffective modalities induced a multisensory cross-modal interaction, while Integrative cells B column demonstrates the number of nigral neurons that reacted to two or three different sensory modalities to a statistically significant extent and additionally exhibited multisensory integration. The last three columns of the table denote the numbers and the distribution of cross-modal interactions within the integrative SN multisensory neurons. V, visual; A, auditory; S, somatosensory.
The inverse effectiveness principle was observed in both structures, i.e. the cells with the weakest net unimodal responses exhibited the strongest enhancement effects. There was a strong significant negative correlation between the strengths of the best unimodal net responses and the percentage enhancements in the CN ($N = 26$, $r = -0.52$, $P < 0.01$) and also in the SN ($N = 28$, $r = -0.39$, $P < 0.01$).

**Effect of multisensory stimulation on the neuronal response onset latencies**

We also investigated the effect of multisensory stimulation on the neuronal response onset latencies. In each facilitatory interaction, the multisensory response onset latency was compared with the onset latency of the best unimodal response. The median response onset latency of the multisensory responses in the CN (median = 50 ms, $N = 26$; range 5–105 ms) was significantly shorter than that of the best unimodal responses (median = 65 ms, $N = 26$; range 15–135 ms; Wilcoxon matched pairs test, $P = 0.02$). A similar effect was observed in the SN, where the multisensory response latency decreased (median = 55 ms, $N = 28$, range 10–115 ms) was significantly shorter (Wilcoxon matched pairs test, $P = 0.03$) than that of the best unimodal responses (median = 70 ms, $N = 28$, range 10–140 ms).

**Discussion**

Our results furnish new data concerning the multimodal representation of the environment in the basal ganglia of the mammalian brain. We recorded single-cell responses to visual, auditory, somatosensory and multisensory stimulation in the SN pars reticulata and the dorsolateral aspect of the CN, and found that multisensory stimulation elicited significantly different responses in the neurons than did the individual sensory components. These results provide a comprehensive picture of the multisensory integration ability of single-neurons in the basal ganglia.

In our sample, a large majority of the sensory CN and SN neurons were multisensory. A similarly, high number of multisensory units (> 50%) were found in the SC, but the number of multisensory units described in the anterior ectosylvian area (AEV; approximately 20%) is much lower (Meredith & Stein, 1986; Wallace et al., 1992; Wallace & Stein, 1996; Stein, 1998; Benedek et al., 2004). Interestingly, through statistical analysis of their responses to separate visual, auditory and somatosensory stimuli, most of the integrative CN and SN units were classified earlier as unimodal. The units responded to only one modality to a significant extent if the modalities were presented alone, but the simultaneous presentation of originally ineffective modalities was able to induce multisensory interactions. Any SN and CN unit that exhibited a significant cross-modal response enhancement or depression were classified as multisensory. Thus, the analysis of the neuronalresponsivity to separate visual, auditory and somatosensory stimulation without any combination of the modalities may have strongly underrepresented the number of multisensory units in the SN and the CN (Pouderoux & Freton, 1979; Magarinos-Ascone et al., 1994; Chudler et al., 1995; Nagy et al., 2005b).

Similarly to earlier findings in the CN, the majority of the investigated multisensory CN and SN neurons displayed a significant...
multisensory interaction (Chudler et al., 1995). Approximately three-quarters of the interactions found in the SN and the CN involved a cross-modal multisensory response enhancement, while the remaining quarter produced a multisensory response depression. Both facilitatory and inhibitory interactions were observed in each bimodal stimulus combination. The magnitudes of the response enhancements and depressions varied widely among the CN and the SN cells. The level was generally under 200%, although there were CN and SN neurons that exhibited extremely strong multisensory effects, with enhancements up to 688% and 574%, respectively. The magnitudes of the multisensory indices calculated in the CN and SN were in the same range as those in the SC, but higher than those in the anterior ectosylvian area (Meredith et al., 1987; Wallace et al., 1992). Additionally, the investigated CN and SN cells displayed very different levels of the strength of the response. Similarly, as described earlier in the SC, both in the SN and in the CN there was an inverse relationship between the response enhancement that the stimuli produced in combination and the effectiveness when they were presented alone (Meredith & Stein, 1986). Hence, the pairing of the least effective or ineffective unimodal stimuli induced a much larger multisensory effect in the basal ganglia neurons than did the pairing of highly effective unimodal stimuli. This suggests that multisensory interactions in the basal ganglia improve the successful detection of environmental stimuli even when the unimodal sensory components presented alone have no significant meaning for the animal.

Stanford et al. (2005) have described a new classification of multisensory interactions in the feline SC. In contrast with the earlier commonly used facilitatory and inhibitory interactions, the multisens-

Fig. 5. Distribution of multisensory indices in the caudate nucleus (A) and in the substantia nigra (B). The black columns denote the percentage enhancement, and the striped columns denote the magnitude of the multisensory response depression. The abscissa reflects the magnitude of multisensory interactions (%), and the ordinate the numbers of interactions.

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sory effects were classified as subadditive, additive or superadditive. The interactions found in the CN and in the SN that were either significantly facilitatory or significantly inhibitory in the classical approach of Meredith & Stein (1986) were recalculated according to the new classification. All the facilitatory interactions in the basal ganglia proved to be either additive or superadditive, but never subadditive, while the inhibitory interactions were consistently subadditive.

The CN and the SN neurons displayed consistently shorter response onset latencies in response to the multisensory than to the separate unimodal stimuli. Thus, our results suggest that there is a faster response to multisensory stimuli even at a single CN and SN cell level than for the separate unimodal components. This is in line with the observations that in humans and in behaving animals there is a substantial decrease in reaction time to multisensory stimulation (Goldring et al., 1996; Frens & van Opstal, 1998; Harrington & Peck, 1998; Giard & Peronnet, 1999; Taylor et al., 1999).

In order to obtain comparable results and to exclude stimulus site-related differences in the multisensory integration, the sensory stimuli were delivered from the same spatial positions throughout the whole study. Thus, we were not able to investigate the effects of varying stimulus disparity on the quality and quantity of the multisensory interactions. In the SC, a multisensory response enhancement was often found when the visual and auditory stimuli originated from the same spatial position, while a multisensory response depression was mainly detected when the spatial disparity of the simultaneously presented auditory and visual stimuli was large (Meredith & Stein, 1986, 1996; Wallace et al., 1996). In contrast with these findings in the SC, the neurons in the CN and the SN often displayed a multisensory response depression to sensory stimuli originating from the same spatial position. We also used a constant stimulus intensity. In general, we employed the intensities that were found optimal for the majority of the sensory CN and SN units in a previous study (Nagy et al., 2005b). Thus, we were again not able to analyse the dependence of the magnitude of the multisensory interactions upon the stimulus intensity.

In the SC, the strongest multisensory response enhancement was detected when the stimulus intensity used was not optimal, i.e. a weak auditory and/or visual stimulus (Meredith & Stein, 1986). In contrast with this, the CN and SN neurons often revealed an extremely intensive multisensory enhancement when the optimal stimulus parameters were applied.

Multisensory integration was detected earlier in the intermediate and deep layers of the SC (Meredith & Stein, 1986; Kadunce et al., 1997, 2001; Stein, 1998; Wallace et al., 1998) and in the AES cortex (Wallace et al., 1992; Benedek et al., 2004). The similar type of interactions revealed in the basal ganglia supports the notion concerning ascending multisensory tectofugal pathways to the CN and to the SN (Nagy et al., 2005b). The caudate body may receive its multisensory afferentation predominantly from the tectum and the AES cortex via the lateralis-medialis-suprageniculate nuclear complex of the thalamus (Norita et al., 1991; Hirting et al., 2001a, b; Nagy et al., 2003). The excitatory multisensory inputs of the SN may originate from the CN (Rodrigue et al., 2000) or from the tectum through direct (Comoli et al., 2003) or indirect pathways (Kita & Kitai, 1987; Redgrave et al., 1987; Tokuno et al., 1994; Lokwan et al., 1999; Jiang et al., 2003). Accordingly, we assume that the CN and the SN, as particular parts of the tecto-thalamo-cortical multisensory network, exert a critical function in multisensory integration. The multisensory integration in the CN and the SN can presumably facilitate the processing of complex sensory stimuli as concerns the sensory feedback of motor actions controlled by the basal ganglia.

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Abbreviations

CN, caudate nucleus; SN, substantia nigra.

References


