Hypnotic manipulation of effort sense during dynamic exercise: cardiovascular responses and brain activation

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Departments of ¹Physical Therapy and ²Radiology and the ³Moss Heart Center, University of Texas Southwestern Medical Center, Dallas 75390-8876; ⁴Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107; and ⁵Department of Kinesiology, University of Wisconsin, Madison, Wisconsin 53706
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Williamson, J. W., R. McColl, D. Mathews, J. H. Mitchell, P. B. Raven, and W. P. Morgan. Hypnotic manipulation of effort sense during dynamic exercise: cardiovascular responses and brain activation. J Appl Physiol 90: 1392–1399, 2001.—The purpose of this investigation was to hypnotically manipulate effort sense during dynamic exercise and determine whether cerebral cortical structures previously implicated in the central modulation of cardiovascular responses were activated. Six healthy volunteers (4 women, 2 men) screened for high hypnotizability were studied on 3 separate days during constant-load exercise under three hypnotic conditions involving cycling on a 1) perceived level grade, 2) perceived downhill grade, and 3) perceived uphill grade. Ratings of perceived exertion (RPE), heart rate (HR), blood pressure (BP), and regional cerebral blood flow (rCBF) distributions for several sites were compared across conditions using an analysis of variance. The suggestion of downhill cycling decreased both the RPE (from 13 ± 2 to 11 ± 2 (SD) units; P < 0.05) and rCBF in the left insular cortex and anterior cingulate cortex, but it did not alter exercise HR or BP responses. Perceived uphill cycling elicited significant increases in RPE (from 13 ± 2 to 14 ± 1 units), HR (+16 beats/min), mean BP (+7 mmHg), right insular activation (+7.7 ± 4%), and right thalamus activation (+9.2 ± 5%). There were no differences in rCBF for leg sensorimotor regions across conditions. These findings show that an increase in effort sense during constant-load exercise can activate both insular and thalamic regions and elevate cardiovascular responses but that decreases in effort sense do not reduce cardiovascular responses below the level required to sustain metabolic needs.

One’s perception of effort during physical exertion, independent of the actual force production, can largely affect the magnitude of the cardiovascular response (15). Cardiovascular responses generally occur in proportion to the intensity of physical activity as a result of medullary integration of both afferent input arising from the working skeletal muscles and descending signals (central command) originating in higher brain regions (32). The difficulty in studying these two mechanisms independently arises from the fact that any actual increase or decrease in the required level of physical exertion can alter both the level of central command and degree of afferent input from the working limb. In an effort to uncouple these mechanisms and identify the potential contributions of higher brain centers toward cardiorespiratory regulation, numerous investigators have successfully employed hypnotic suggestion to selectively alter subjects’ perceived level of exertion or effort sense during constant-load exercise (2, 17–19). Of note, “effort sense” may be the more appropriate terminology when describing these hypnotically induced changes as opposed to central command as classically defined. Central command typically implies a feed-forward mechanism involving the parallel activation of both motor and cardiovascular centers, and this specific mechanism may not be involved during hypnotic suggestion. Thus hypnotically induced cardiorespiratory alterations have been attributed to the selective activation of higher brain centers involved in the integration of effort sense.

The cerebral cortical structures and their roles in the complex process of establishing or modifying the cardiovascular response for a given level of sensory input on the basis of the exercise intensity are not well understood. Neuroimaging studies employing hypnotically induced perceptual changes have identified cortical regions related to the integration of sensory information, including the sensorimotor cortex, anterior cingulate cortex, insular cortex, and thalamus (11, 25). Additionally, imaging studies performed during exercise have reported that the insular cortex may play a significant role in cardiovascular regulation (20, 34, 35). The insular cortex has neural connections to numerous subcortical regions involved in cardiovascular regulation (5, 27, 37) and has further been implicated in the scheme of blood pressure (BP) regulation and baroreflex sensitivity (28, 38). As well as its role in

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autonomic regulation, the insular cortex also serves as a site of sensory integration, and it has connectivity with numerous limbic structures (29, 37). It is possible that the insular region may serve to modulate cardiovascular responses based on an individual’s level of perceived effort. This perceptual information, together with the actual metabolic and mechanical afferent signals arising from the exercising skeletal muscle, would then converge at subcortical sites to dictate an overall cardiovascular response.

The purpose of this investigation was to hypnotically manipulate effort sense during exercise and determine whether cerebral cortical structures previously implicated in the central modulation of cardiovascular responses were activated. Regional cerebral blood flow (rCBF) distribution in the insular cortex and several other cortical regions was assessed during exercise using single-photon-emission computed tomography (SPECT). The SPECT technique measures rCBF distributions that reflect increases or decreases in local metabolic demand due to local neuronal activation or deactivation, respectively (24). This technique is uniquely suited for large-muscle exercise because it employs a retained brain blood flow tracer, which can be injected during exercise. Actual brain scanning can be performed at a later time, but images obtained reflect patterns of cerebral activation during exercise (at the time of injection). We hypothesized that hypnотically induced increases or decreases in effort sense during constant-load exercise would result in increases or decreases, respectively, in insular cortex rCBF distribution.

METHODS

Subjects. A total of 43 individuals initially volunteered to participate in this experiment, and each of these volunteers completed a battery of psychological questionnaires consisting of the 1) State-Trait Anxiety Inventory (31), 2) Profile of Mood States (14), 3) Beck Depression Inventory (3), and Eysenck Personality Questionnaire (7). Individuals scoring two or more standard deviations above the published norms for anxiety, depression, neuroticism, or psychoticism, as measured by these inventories, were not eligible to participate in the present study. All participants provided written informed consent before their participation in this study approved by the University of Texas Southwestern Medical Center Institutional Review Board and the Environmental Health and Safety Committee.

Of the 43 individuals who completed the aforementioned scales, 25 volunteered to take part in a subsequent screening designed to measure hypnotizability. The Harvard Group Scale of Hypnotic Susceptibility (HGSHS) (31) was administered to the subgroup of 25 subjects, and the mean hypnotizability score for this sample was 7.4. Fifteen of the twenty-five subjects then participated in a hypnotic deepening session that was based on a modification of the induction procedures described in Form C of the Stanford Hypnotic Susceptibility Scale (33). The verbatim induction is available in the briefing. Seven of the ten individuals volunteered to complete the exercise portion of the study, but one subject was withdrawn on the basis of radiation exposure. The remaining six individuals completed all of the exercise trials as described in this study. The mean HGSHS score for this subgroup was 9.67, and this level of hypnotizability was higher than the mean value of 6.33 for nonparticipants (effect size = 1.40). The group of six participants forming the experimental group did not differ from the nonexperimental group on any of the remaining psychological variables (i.e., state anxiety, trait anxiety, depression, mood states, extroversion, neuroticism, or psychoticism).

The four women and two men (aged 25 ± 2.8 yr) undergoing the exercise protocols were all in good health and reported participation in a regular exercise program (from 3 to 5 days/wk) for at least the past 6 mo. All were normotensive (resting BP <140/90 mmHg), and none was taking any cardiovascular medications or reported any history of cardiovascular or neurological disorders. Poststudy medical examination of individual magnetic resonance (MR) scans showed no significant abnormalities.

Hypnotic procedures. The induction procedure was identical under all experimental conditions. The baseline condition was always conducted first, and the uphill and downhill trials were rotated (i.e., up-down or down-up) and randomly assigned. Participants were informed before a given ride that they would be asked to imagine an uphill or downhill grade during the final 5 min of their 15-min exercise bout. In other words, they were told in advance that the final portion of exercise on a given day would be more or less effortful than the control condition. It was necessary to take this approach because participants would always know what the third ride would involve once the second had been completed. It is possible that individuals may have had an anticipatory response as a consequence of this prior knowledge, but this approach was deemed as necessary to facilitate consistency in perceptual-cognitive responses across trials.

The induction procedure employed in each case consisted of reminding the individual that it would be possible to cycle continuously for 15 min, provide verbal ratings of perceived exertion (RPE) periodically, and remain hypnotized throughout the session. Subjects were instructed to cycle at a cadence of 50–60 rpm and were paced by an investigator so as to maintain a constant cadence across conditions. The suggestions of either “downhill or uphill” cycling were initiated at minute 10 and continued over the last 5 min of exercise. Subjects were asked to imagine the appearance of an uphill or downhill grade off in the distance, and they were also asked to nod their head when they could see the approaching grade. Suggestions were continued until this ideomotor commitment (i.e., head nod) was made. All subjects acknowledged the imaginary grade change before the actual onset of the grade change (at minute 10). This approach ensured that there would be no variation in exercise duration at the time of brain blood flow tracer injection when subjects were perceiving the grade change.

Exercise procedures. Each 15-min exercise condition was divided into three, 5-min periods for data collection. Data were recorded at rest and during exercise over the last 2 min of each period. These three measurement periods will be referred to as time periods 5, 10, and 15 min for convenience in comparing data across conditions. Male subjects cycled at a constant workload of 100 W and female subjects at 75 W. Seat height and handlebar position used for the first condition were recorded and used for subsequent tests. Heart rate (HR) was recorded by palpation of the radial artery for 1 min, and BP measurements were taken by auscultation from the upper arm by an experienced investigator. RPE were also...
obtained during exercise using the 6–20 category scale developed by Borg (4) for use in quantifying the overall effort sense, as well as fractionated ratings for the legs and upper body. Injection of the blood flow tracer occurred during the 15-min time period (actual injection at minute 13) so as to determine rCBF distribution during perception of changes in effort.

*rCBF* assessment. On day 1, each subject was familiarized with all procedures and methodologies to be used during the study. A venipuncture was made in the antecubital vein of the left arm using a 21-gauge over-the-needle Teflon catheter ~20 min before testing. The needle was removed, and the catheter was left in place and capped with an injectable site to facilitate the innocuous administration of the retained blood flow tracer.

To determine the rCBF distributions during each testing condition, 20 mCi of freshly reconstituted 111mTe-ethyl cysteinate dimer (Neurolit, DuPont Pharma) was injected intravenously. This retained brain blood flow tracer is a photon emitter with a physical half-life of 6 h. Increases in rCBF to a particular region of the brain subsequently lead to an increase in the amount of radioactivity recorded from that region (8, 9, 12). A technician administered the blood flow tracer and flushed the catheter with normal saline. The subjects continued their activity for an additional 2 min to facilitate appropriate distribution of the tracer. Because their eyes were closed during exercise, subjects were unaware of the exact time of injection and reported no noticeable side effects. All subjects were taken to the SPECT camera room 20 min after exercise, and imaging was completed within 50 min of injection for all subjects.

The brain scans were obtained with a fast-rotating three-headed SPECT scanner (model 3000, Picker, Cleveland, OH). The subjects were placed in the camera with their head held in position using a forehead strap and a chin strap. A trained technician optimally positioned the cameras, and the exact coordinates were recorded for subsequent scans. The process was repeated for each of the test protocols on separate days. Acquired data were fan beam and uniformity corrected. Im- ages were reconstructed in the transaxial plane, and a three-dimensional postprocessing low-pass filter was then applied. Coronal and sagittal images were generated from the transaxial image set, which was corrected with an angle parallel to the orbitomeatal line. Images were displayed at a thickness of four pixels (~7 mm). SPECT images were then transferred over the campus network to a computer workstation (Tru64Unix, Compaq, Houston, TX) equipped with image analysis software (AVS, Advanced Visual Systems, Waltham, MA).

On a separate occasion, each subject also underwent a MR scan. A 1.5-T system (Gyroscan NT, Philips Medical Systems, Shelton, CT) was used to obtain ~100 contiguous, 1.5-mm-thick gradient-echo axial slices. Each individual’s MR images were then transferred over the campus network to the workstation for coregistration with SPECT rCBF data.

**Image processing and statistical analysis.** Data processing involved coregistration of each individual’s SPECT scans, obtained during the exercise protocols, to the scan obtained during the control trial so that total counts were equal for all volumes. This was done using an automated volume coregistration algorithm widely used for positron-emission tomography (PET)-PET coregistration (36). Each individual’s brain images were aligned in three dimensions by computer. Once the SPECT scans for a given subject were coregistered, normalization of total radioactive count variability was obtained by rescaling each volume so that total counts were equal for all volumes.

After SPECT-SPECT coregistration for each individual, SPECT-MR coregistration was obtained using an interactive coregistration algorithm (14) implemented on the workstation, after the SPECT voxel size was made to match the MR voxel size. Compared against the baseline SPECT, absolute and percent count differences for each pixel in the other two scans were obtained. These differences were then displayed, for a selected slice within the volume, as a color overlay superimposed on the MR image.

The right and left insular regions were located using the coregistered MR image as an anatomic reference. Using the computer, regions of interest (ROIs) were drawn around the insular region as seen on the MR slice. This procedure was repeated on contiguous transaxial slices until the entire insula had been assessed. The number of 1.5-mm slices ranged from 16 to 22 across all subjects. On the basis of the findings reported by Oppenheimer et al. (21), who demonstrated select regions of cardiovascular representation, which appeared to be located in the inferior insular, coupled with the 8- to 10-mm spatial resolution for this technique, we chose to divide the insular cortices into equal halves representing superior and inferior regions. The number of radioactive SPECT counts within the inferior regions for the right and left insular cortices were then compared across the three conditions for each subject as absolute counts and as percent changes from the baseline condition. Additionally, ROIs were drawn around leg sensory motor areas, hand and forearm sensory motor regions, thalamus (divided bilaterally), anterior cingulate cortex, and a white matter region encompassing the anterior corpus callosum for all trials. The SPECT data were corrected to the baseline condition for any changes in rCBF to white matter regions. Additionally, a region of gray matter approximating Brodmann’s area 44, not believed to be differentially affected by the hypnotic protocol, was assessed to determine the effects of potential changes in breathing (i.e., PCO2) on global CBF (gCBF). During the processing and rCBF data assessment, data were coded such that the researchers performing these analyses were blinded with regard to the order of experimental conditions.

Data collected during the three trials were tested for normality and subsequently analyzed using a Friedman’s nonparametric analysis of variance with a main effect of experimental condition. If significant *F* ratios were detected, a Student-Newman-Keuls post hoc analysis was used to determine specific mean differences. The alpha level was set at *P* < 0.05 for all analyses.

**RESULTS**

**Hypnosis.** The hypnotic induction performed while the subjects were seated on the bicycle required an average time of 5.9 ± 0.05 (SD) min (range 5.0–6.8 min). During the debriefing that followed each exercise trial, subjects were asked to estimate the amount of time that had elapsed, and the average time was 17.4 ± 7.6 min (range 10–33 min). The actual mean time was 22 min, and the difference of 4.6 min yielded an effect size of 1.12. Although this effect size is significant and in the predicted direction, it is not as great as probably would have been the case for a relaxed hypnosis condition. Nevertheless, the time distortion frequently reported for hypnosis was apparent here even though the subjects were active for 15 of the 22 min.

During the debriefing session after the downhill and uphill exercise sessions, subjects were asked to rate the
vividness of the hypnotic condition on a 10-point category scale ranging from 1 (not at all vivid) to 10 (very vivid). The mean rating for the downhill session was 7.17 compared with a rating of 8.33 for the uphill session, and this yielded a large effect size of 1.05. Hence, the perceived vividness of the hypnotic suggestion was greater for the uphill condition.

Cardiovascular and rCBF responses. The control condition involved the subjects cycling at a constant workload under hypnosis with the perception of cycling on a level grade. The RPE and cardiovascular data are presented in Figure 1. Resting HR averaged ±68 ± 9 (SD) beats/min and mean BP was 88 ± 9 mmHg. During this exercise condition, the overall RPE values for the 5- and 10-min periods were 11 ± 0.7 and 13 ± 0.5 units, respectively. The RPE for the legs at 5 min was 10 ± 1 units and was 12 ± 1 units at 10 min. The RPE value for the chest remained constant at 12 ± 1 units. During minute 15 of this condition, overall RPE was 13 ± 2 units, leg RPE was 12 ± 1 units, HR was 122 ± 11 beats/min, and mean BP was 93 ± 10 mmHg (Fig. 1). Changes in rCBF distribution are presented in Table 1 as radioactive counts (within the ROI) and as a percent change from control for the downhill and uphill conditions.

For the perception of downhill cycling, subjects were told that they were going down a hill after data collection for the 10-min period was completed. There were no significant changes for any variables at the 5- or 10-min periods between conditions (Fig. 1). However, the overall RPE value during minute 15 of exercise was significantly lower compared with the same period of the control condition (11 ± 1 vs. 13 ± 2 units; \( P < 0.05 \)). Similarly, both the leg RPE (10 ± 2 units) and chest
respectively. The images in the center show activation seen in sagittal magnetic resonance imaging data for the whole brain. The single-positron-emission computed tomography scale with a positive range from 5 to 25% (from green through yellow to red) and negative range from −5% to −25% (from purple through dark blue to light blue). The white lines denote the specific regions of interest assessed (in this brain slice) and encompass the insular cortices, thalamic regions (bilaterally) and anterior cingulate cortex. Changes in regional cerebral blood flow were mapped on the magnetic resonance image using an arbitrary color scale with a positive range from 5 to 25% (from green through yellow to red) and negative range from −5% to −25% (from purple through dark blue to light blue). The white lines denote the specific regions of interest assessed (in this brain slice) and encompass the insular cortices, thalamic regions (bilaterally) and anterior cingulate cortex.

Table 1. Changes in regional cerebral blood flow distribution

<table>
<thead>
<tr>
<th>Cortical Region</th>
<th>Control</th>
<th>Downhill</th>
<th>Uphill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg sensorimotor</td>
<td>821 ± 84</td>
<td>814 ± 81 (−0.9 ± 3%)</td>
<td>815 ± 76 (−0.7 ± 3%)</td>
</tr>
<tr>
<td>Right arm sensorimotor</td>
<td>716 ± 110</td>
<td>697 ± 108 (−2.6 ± 3%)</td>
<td>721 ± 111 (0.7 ± 5%)</td>
</tr>
<tr>
<td>Left arm sensorimotor</td>
<td>709 ± 99</td>
<td>712 ± 102 (0.4 ± 4%)</td>
<td>704 ± 107 (−0.6 ± 5%)</td>
</tr>
<tr>
<td>Anterior cingulate cortex</td>
<td>655 ± 100</td>
<td>612 ± 106 (−6.6 ± 4%)</td>
<td>685 ± 117 (4.6 ± 3%)</td>
</tr>
<tr>
<td>Right thalamic region</td>
<td>618 ± 97</td>
<td>631 ± 92 (2.1 ± 5%)</td>
<td>675 ± 104 (9.2 ± 4%)</td>
</tr>
<tr>
<td>Left thalamic region</td>
<td>614 ± 94</td>
<td>605 ± 96 (−1.3 ± 3%)</td>
<td>623 ± 100 (1.6 ± 4%)</td>
</tr>
<tr>
<td>Right superior insular cortex</td>
<td>614 ± 77</td>
<td>593 ± 80 (−3.4 ± 5%)</td>
<td>619 ± 85 (0.8 ± 4%)</td>
</tr>
<tr>
<td>Right inferior insular cortex</td>
<td>617 ± 65</td>
<td>608 ± 83 (−1.5 ± 6%)</td>
<td>665 ± 85 (7.7 ± 4%)</td>
</tr>
<tr>
<td>Left superior insular cortex</td>
<td>625 ± 51</td>
<td>616 ± 83 (−1.3 ± 4%)</td>
<td>633 ± 59 (1.2 ± 4%)</td>
</tr>
<tr>
<td>Left inferior insular cortex</td>
<td>621 ± 64</td>
<td>572 ± 68 (−7.9 ± 4%)</td>
<td>635 ± 88 (2.4 ± 6%)</td>
</tr>
<tr>
<td>Brodmann’s area 44</td>
<td>705 ± 68</td>
<td>714 ± 68 (1.3 ± 1%)</td>
<td>692 ± 88 (−1.9 ± 1%)</td>
</tr>
<tr>
<td>Corpus callosum (white matter)</td>
<td>448 ± 45</td>
<td>454 ± 55 (1.1 ± 2%)</td>
<td>441 ± 88 (−1.6 ± 2%)</td>
</tr>
</tbody>
</table>

Values are means ± SD given as radioactive counts within the region of interest (ROI) and as percent change from control for the downhill and uphill conditions (within parentheses). *P < 0.05.

RPE (10 ± 3 units) were reduced. There were no significant changes in HR (119 ± 10 beats/min) or mean BP (92 ± 11 mmHg) compared with minute 15 of the control ride. There were no significant differences for rCBF distributions in the hand or leg sensory motor regions between control and perceived downhill cycling (Table 1). There was a decrease in rCBF for the left inferior insular region (−7.9 ± 4%; P < 0.05) but no significant changes for the right insular or thalamic areas. The perceived downhill cycling also elicited a significant decrease in the anterior cingulate cortex (−6.6 ± 4%; P < 0.05) (Fig. 2).

Although there were no significant changes for minutes 5 and 10, during the 15-min time period of constant-load exercise when the subjects perceived that they were cycling up a hill, the RPE for the legs was significantly elevated from the control condition (13 ± 1 units; P < 0.05). Both overall RPE (14 ± 2 units) and chest RPE (13 ± 2 units) were significantly higher than the perceived downhill cycling condition for the same period. During the minute 15 time period of exercise, when the suggestion of uphill cycling was initiated, both HR (138 ± 14 beats/min) and mean BP (100 ± 11 mmHg) were significantly...
elevated. No significant differences were observed for hand or leg sensory motor regions as compared across conditions (Table 1). There was a significant increase in rCBF distribution for the right inferior insular region (+7.7 ± 4%; \( P < 0.05 \)) and also in the right thalamus (9.2 ± 4%, \( P < 0.05 \) ) (Fig. 2). There were no significant changes in any of the other cortical regions assessed during uphill cycling (Table 1).

**DISCUSSION**

The primary findings from this investigation were that hypnotic manipulation to increase effort sense during constant-load exercise elevated both HR and BP as well as increased activation in the right insular cortex and right thalamic regions. On the other hand, reductions in effort sense decreased activation in the anterior cingulate cortex and left insular cortex but did not produce a fall in HR or BP. Cortical activation of both hand and leg sensory motor regions remained constant across hypnotic conditions. Taken together, these data imply that the cerebral cortical structures presently found to be activated by increases in effort sense during exercise may be related to the augmented cardiovascular responses; however, their deactivation did not diminish the cardiovascular responses during exercise. It is possible that the BP cannot be driven below some minimally required level as dictated by afferent input from the working skeletal muscle. Such a contention, as originally forwarded by Morgan et al. (18), would appear plausible considering the redundancy of the cardiovascular neural control system regarding input from both higher brain centers and active skeletal muscle toward the overall cardiovascular regulation (15). The patterns of cortical activation and structures involved are consistent with related investigations and may provide further insight into the role of the cerebral cortex in establishing exercise-induced cardiovascular responses.

In evaluating the overall findings of this study with respect to related investigations involving hypnosis and/or exercise, there is considerable consistency between the reported perceptual and cardiovascular responses, as well as the specific cerebral cortical regions involved. Previous hypnosis studies have reported that the "suggested load" had a significant effect on both cardiovascular (2, 18) and respiratory responses (2, 17–19), although the well-studied respiratory changes were not a focus of this investigation. It should also be mentioned that not every exercise-related hypnosis study has yielded significant cardiorespiratory changes (10), and such inconsistencies may be more related to the specific methodologies or protocols employed. Although this study does not attempt to assess the effects of the hypnotic state "per se" compared with a nonhypnotic state, the specific findings regarding patterns of brain activation as a consequence of the hypnotic manipulation of effort sense serve as the focus of our discussion.

The suggestion of downhill cycling produced decreases in rCBF distribution in both the anterior cingulate cortex and left insular cortex as shown in Table 1. Deactivation of the anterior cingulate cortex has been consistently reported in studies using hypnotic analgesia to reduce pain (11). Although our subjects did not report any leg pain during exercise, the differential RPE related to the lower extremities was significantly reduced by the suggestion of downhill cycling. Rainville et al. (25) have further demonstrated that activity in the anterior cingulate closely parallels a selective change in the perceived unpleasantness of painful stimuli. It is important to note that whereas pain and perceived exertion (or effort sense) are two very distinct concepts, they both represent a form of "subjective" sensory input and therefore may be processed or integrated in similar areas of the brain. Our subjects were able, through hypnotic manipulation of effort sense, to selectively alter their sensation of effort as referenced from the working limbs. Furthermore, there were no significant changes at the leg sensorimotor cortex during hypnotic suggestion. This implies that activation of the sensorimotor cortex may be more dependent on the level or type of afferent neural input from the working muscle (e.g., local mechanical and metabolic influences) as opposed to one's subjective perception of the sensations related to this afferent activity.

The suggestion of downhill cycling also elicited a reduction in rCBF distribution to the left insular cortex. Of note, it has been suggested that the left insular cortex is involved in the regulation of parasympathetic activity (21). Decreases in insular activity have previously been related to increases in resting BP (35, 38). However, the insular deactivation noted during exercise was not coupled with a significant change in HR or BP. It appears that the afferent input from the periphery may serve to set a minimal level of cardiovascular response and cannot be further diminished by decreasing central influences from higher brain centers. In agreement with this contention, Duncan et al. (6) reported that BP elevations maintained by postexercise cuff occlusion could not be lowered using hypnosis. There are numerous investigations demonstrating the ability of afferent input from the working limbs to elevate BP (1, 16). Thus a centrally mediated reduction in left insular cortex rCBF distribution during exercise cannot override the excitatory cardiovascular responses evoked by contraction-sensitive skeletal muscle afferents.

When subjects were given the suggestion of uphill cycling, there were significant increases in rCBF distribution to the right thalamic region and right insular cortex, as well as elevations in both HR and BP. Although the thalamus is composed of numerous nuclei, each with discrete functions, we included the entire thalamus for analysis to ensure adequate spatial resolution given our methodology. Under our experimental conditions, thalamic activation is most likely a result of alterations in sensory input as related to the elevated rating of perceived exertion during suggested uphill cycling. Additionally, regions of the thalamus have been implicated in cardiovascular regulation and
integration of afferent baroreceptor information (22). The limitations of our methodology and protocol do not allow us to clarify a specific role for the thalamus beyond its involvement as one of several cortical structures related to the hypnotically induced changes.

Activation of the insular cortex has been reported during volitional exercise and may further be related to the resulting cardiovascular responses (20, 34, 35). The right insular cortex has been suggested to be involved in the regulation of sympathetic nervous activity (21). It has also been proposed that the insular cortex may serve as a site of “central command” involving the feed-forward signals and, as previously defined, eliciting parallel activation of cardiorespiratory and motor areas. Although insular activation was related to cardiovascular excitation during the suggestion of uphill cycling at a constant workload, there were not parallel changes in leg sensorimotor regions. This observation raises the issue of whether effort sense or perceived exertion are appropriate terminology to be used synonymously with central command.

In this investigation, the insular cortex, with both autonomic (27, 37) and limbic connections (29), appears to be responding to an individual’s sense of effort during exercise and may further act to modify cardiovascular responses accordingly. It has been suggested that the insular cortex may be involved in BP regulation. The insular cortex has reciprocal connections with multiple brain stem nuclei, including a region of the nucleus tractus solitarii innervated by baroreceptor afferents (27). Data from Saleh and Connell (28) and Zhang et al. (38) have demonstrated a role for the insular cortex in the modulation of baroreflex sensitivity. It has also been shown that central command can act to reset the arterial baroreflex during exercise (23). Although we cannot provide direct evidence linking the insular cortex to centrally mediated changes in baroreflex function at present, activation of this cortical region may be related to an exercise or effort-initiated resetting of the arterial baroreceptors known to occur with physical activity.

Limitations. With respect to the potential limitations of our study, no specific testing was performed to assess hemispheric dominance and the areas of the brain assessed were dictated by the limits of the spatial resolution of the technique. Traditionally, the hemisphere that manages language is called the dominant hemisphere and, in ~95% of the population, the left hemisphere is dominant. Although it appears that some degree of laterality exists for autonomic function with respect to low- and higher intensity exercise, studies on persons with right hemispheric dominance could potentially yield different results with respect to patterns of insular activation. Because of the spatial limitations of the SPECT technique (~10 mm) we cannot assess, with confidence, smaller cortical regions that may also play a role in effort sense and cardiovascular regulation. Thus the cerebral cortical regions identified in this study are probably not inclusive of all regions involved in the hypnotic manipulation of effort sense.

Changes in Pco2 or end-tidal Pco2 (Petco2) can alter gCBF and in turn systematically alter rCBF (26). Although we would expect no significant PCO2 between the control ride and perceived downhill cycling, the perception of uphill cycling should have increased ventilation, on the basis of prior findings, which could in turn decrease Petco2 values. As one would expect, a decrease in gCBF with a decrease in Pco2, we may have underestimated the actual increases in rCBF occurring during this condition. Although no direct measures of Pco2 or Petco2 levels were made, we assessed a gray matter region (approximating Brodmann’s area 44) as another means of determining the effects of exercise and possible Pco2 decreases on rCBF and found no significant changes (Table 1). Additionally, correcting for these small changes (in lieu of using white matter changes) did not alter the findings or conclusions of this investigation.

Conclusions. The hypnotic manipulation of effort sense during dynamic exercise can significantly alter patterns of brain activation and elicit cardiovascular changes. Our findings suggest that the insular cortex, thalamus, and anterior cingulate cortex are important cerebral cortical structures involved in the process of integrating one’s effort sense and may further contribute toward affecting appropriate cardiovascular adjustments during physical activity. Increases in effort sense elevated both HR and BP, yet reductions in effort sense did not decrease either variable. This lack of cardiovascular change, in response to a decreased effort sense, serves to confirm the importance of afferent input from the exercising skeletal muscle in establishing the magnitude of cardiovascular response required to sustain a given metabolic demand. Although these data cannot address a specific mechanism involved in the cardiovascular changes resulting from an increase in effort sense during constant-load dynamic exercise, we would postulate an alteration in the arterial baroreflex.

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