WHAT IS SMOOTH PURSUIT?

Smooth pursuit reflects a conjugate eye movement system that has developed to take full advantage of the high acuity properties of the fovea. Each of these systems uses its own unique neuroanatomic circuitry before entering the final common pathway at the level of the ocular motor nuclei. The pursuit system in particular depends on cerebral cortical processing, which synthesizes a neural representation of stimulus motion.

Strictly speaking, smooth pursuit functions to stabilize images of small, moving objects upon the fovea. However, the pursuit system is also chiefly responsible for generating slow phases of optokinetic nystagmus (OKN), which limit full-field motion of the visual environment upon the retina during head movement. In addition, much of the neural machinery of the pursuit system contributes to the suppression or enhancement of the VOR by visual inputs. Dysfunction of smooth pursuit, OKN slow phases, and visual modulation of the VOR nearly always parallel each other in patients.

NORMAL PURSUIT PHYSIOLOGY AND ITS MEASUREMENT

Visual input is required to activate smooth pursuit, since the ability to produce voluntary smooth eye movements in darkness, in contrast to saccades, is quite limited. Pursuit initiation is evoked by motion of an image over the retina; the principal signal that seems to be used is image velocity, also known as retinal slip. The goal of the pursuit system is to generate a smooth eye velocity that matches image velocity, though this match is seldom perfect. About 125-150 msec after the onset of stimulus motion, pursuit begins as a smooth eye acceleration that typically brings the eyes near the velocity of the target within 300 msec of its onset (see Figure 1 for illustration of normal pursuit initiation response). Due to the response latency of pursuit, the first 100 msec or so of the initial pursuit acceleration is based on retinal motion that took place before the eyes began to move. After eye velocity has approximated target velocity, smooth pursuit can be maintained despite relatively small amounts of residual retinal slip. To achieve a stable eye velocity, pursuit maintenance may utilize feedback of a copy of the smooth eye movement command to construct a representation of stimulus motion in space.

The stimuli most commonly used for examining smooth pursuit in the laboratory have either sinusoidal or step-ramp waveforms (Table 1). Sinusoidal stimuli are the gold standard of clinical pursuit measurement. These targets oscillate in a regular, predictable sine wave pattern with respect to time (not space). They measure smooth pursuit maintenance (see Figure 2 for example of sinusoidal pursuit response). Bedside assessment of the pursuit system, usually accomplished by having the patient track the examiner’s slowly moving finger, replicates this stimulus pattern. Normal subjects should be able to follow a target moving back-and-forth every two to four seconds through an amplitude of 20° to 40°, using chiefly smooth eye movement. When the pursuit system alone cannot keep up with stimulus motion, saccades are generated to bring the desired image near the fovea. Failure to accurately follow objects with smooth eye motion thus results in an excessive number of interposed saccades. The resultant attempt at tracking has a jerky, cogwheeling appearance (so-called saccadic pursuit). Smooth pursuit maintenance is traditionally measured by dividing smooth eye velocity by target velocity to obtain a value for pursuit gain. A gain value of 1.0 represents ideal smooth pursuit. Normal pursuit gain depends strongly on the nature of stimulus motion parameters. Target acceleration is the chief determinant of responses to sinusoidal motion; targets of high frequency and amplitude have high accelerations and evoke smooth pursuit having low gain values. The pursuit system is also restricted in that it can only deliver peak smooth eye velocities of about 100°/sec. Smooth pursuit is thus considerably slower than saccades or the VOR, which can each attain velocities of over 500°/sec. This velocity constraint is probably due to sensory processing limitations for visual motion.
Figure 2. Pursuit maintenance response to a 10°, 0.5 Hz sinusoidal stimulus motion in a patient with right frontal infarction. Eye and target position are plotted against time. Leftward (downward) target motion is tracked almost exclusively with smooth eye motion, while rightward motion evokes saccades with a very limited component of smooth tracking. This is an example of an ipsidirectional pursuit defect in a patient with localized cerebral damage. Reprinted with permission from Ref. 48.

**TABLE 1. COMPARISON OF SMOOTH PURSUIT TESTING METHODS**

<table>
<thead>
<tr>
<th>Sinusoidal stimuli</th>
<th>Step-ramp stimuli</th>
</tr>
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<tbody>
<tr>
<td>very predictable</td>
<td>can be made unpredictable</td>
</tr>
<tr>
<td>test pursuit maintenance (steady-state gain)</td>
<td>test pursuit initiation (acceleration, latency)</td>
</tr>
<tr>
<td>a standard procedure</td>
<td>less commonly available</td>
</tr>
<tr>
<td>easily analyzed</td>
<td>individual responses must be analyzed</td>
</tr>
<tr>
<td>tests only perifoveal retina</td>
<td>can spot-test extrafoveal retina</td>
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Step-ramp targets measure initial pursuit acceleration and latency and allow an examiner to project a moving stimulus onto the extrafoveal retina; the initial portion of the evoked pursuit response is then based on information originating from a chosen area of visual field. A disadvantage of this type of testing is that each response is short-lived; many responses must be measured to give consistent results and each response must be analyzed individually. On the other hand, step-ramp targets, unlike sinusoidal stimuli, can be made entirely unpredictable, minimizing the significant contributions of predictive smooth eye movement mechanisms to visual tracking.26,36,42

THE ANATOMY OF SMOOTH PURSUIT

Smooth pursuit processing begins in the retina, where ganglion cells begin to condense some of the raw information coming from the photoreceptors. Current theories of visual processing propose two parallel, anatomically distinct pathways that analyze different aspects of the seen world.74 This dual-pathway model is supported by functional neuroimaging65 and psychophysical investigations in humans. In monkeys, there are at least two distinct retinal ganglion cell types; those projecting to the parvocellular layers of the lateral geniculate nucleus (LGN) carry signals best suited for color and form detection, while those reaching the magnocellular layers are ideal for spatial and motion processing. Functional specialization continues in the cerebral cortex, where visual processing progresses through a series of stages, with increasingly complex neuronal responses at each level. The magnocellular and parvocellular information streams project to distinct zones of striate (primary visual) cortex, then on to specialized zones of peristriate cortex. The magnocellular stream continues in an occipital cortical area designated MT and in the adjacent area MST.38 The human homologue of the MT/MST region lies near the junction of the lateral occipital, temporal and parietal lobes. This homology has been demonstrated by studies in patients with cerebral damage43,45 by functional neuroimaging68,77 and by myeloarchitectonic similarities8 (see Figure 3 for map of cortical regions involved in human smooth pursuit control).

Figure 3. Locations of human cerebral cortical areas participating in smooth pursuit. Arrows indicate principal direction of information flow. Abbreviations: PEF, frontal eye field; STP, superior temporal polysensory area homologue; MT, middle temporal area homologue; MST, middle superior temporal area homologue; PPC, posterior parietal cortex; PVC, primary visual cortex (includes striate and peristriate regions).
The posterior parietal and anterior superior temporal cortex are likely to participate in human smooth pursuit (see Figure 4 for flow diagram of probable human pursuit processing sequence). In monkeys, areas MT and MST project forward to parietal areas 7a and VIP and to an anterior temporal region designated STP. VIP appears to be involved directly in visual motion processing, while areas 7a and STP are extensively interconnected with higher level visual processing areas and probably contribute to the control of visual attention. In humans, both posterior parietal and anterior superior temporal regions show increased blood flow during smooth pursuit and posterior parietal cortex is active during selective attention to moving targets.

Figure 4. Putative smooth pursuit pathway in humans. Abbreviations as above, and: MLGN, magnocellular lateral geniculate nucleus.

The frontal lobes also play an important role in smooth pursuit control. The simian frontal eye fields (FEF) receive substantial projections from the MT/MST region. Neurons in the FEF are active during smooth pursuit and electrical stimulation of these neurons produces ipsilateral smooth eye motion. Cells within the supplementary motor area of monkeys fire selectively with smooth pursuit eye movement, especially when target motion is predictable. The human FEF shows increased blood flow during smooth pursuit.

En route to the brainstem, corticofugal pathways from the simian MT/MST region descend through the pulvinar and posterior capsular area. Frontal corticofugal axons probably traverse the internal capsule as well. Both MST and FEF project to the pontine nuclei, including the dorsolateral pontine nucleus. Purkinje cells in the flocculus and vermis receive signals related to eye motion, head motion, and retinal image motion and they appear to encode a signal proportional to desired pursuit eye velocity.

Floccular and vermal Purkinje cells send inhibitory projections to the ipsilateral vestibular nuclear complex and fastigial nucleus, respectively. The fastigial nucleus sends an excitatory projection to the ipsilateral vestibular nuclei. Cerebellar corticofugal circuits probably drive horizontal pursuit through their inhibitory projections, by reducing the firing rates of vestibular nuclear neurons that drive smooth eye motion in the direction opposite the desired pursuit eye movement. The excitatory contralateral projection known to connect the vestibular nuclei to the abducens nucleus fits this scheme and would complete a double decussation of the horizontal pursuit control circuit. Signals for vertical pursuit project from cerebellar Purkinje cells to the pretectum through the medial longitudinal fasciculus (MLF) and brachium conjunctivum in monkeys. The interstitial nucleus of Cajal (INC) contains neurons that fire during vertical pursuit.

### DISORDERS OF SMOOTH PURSUIT

As outlined above, the smooth pursuit system uses a widespread neural network for sensory input and motor control. It is therefore sensitive to dysfunction nearly anywhere in the brain. A broad range of neurologic disorders, including focal and diffuse cerebral, cerebellar, basal ganglionic, and disease may cause symmetric impairment of smooth pursuit in all directions (Table 2). The basis of pursuit dysfunction in diseases of the basal ganglia is unclear, since the role of these structures in smooth pursuit control has not been defined. Schizophrenia and affective disorders have also been associated with omnidirectional pursuit impairment. Sedative-hypnotic and anticonvulsant drugs may cause symmetric loss of pursuit function, as can normal physiological conditions like inattention, fatigue and senescence.

In contrast to omnidirectional pursuit impairment, asymmetric smooth pursuit always indicates focal neural
The types of pursuit asymmetry identified in patients with focal brain lesions mirror the organizational patterns of the pursuit pathways. Thus, asymmetric responses may occur with respect to: 1) the direction of smooth pursuit; 2) the retinal hemifield of target motion; and 3) the field of gaze in which eye movement takes place. The focal pursuit abnormality most familiar to clinicians is a directional asymmetry in which pursuit is impaired in one horizontal direction compared to the other. This type of defect can be identified on bedside testing. When localized to the cerebrum, it indicates damage in the hemisphere ipsilateral to pursuit impairment. Human cerebral lesions associated with ipsidirectional smooth pursuit dysfunction have typically included either the MT/MST homologue or its descending projections in subcortical white matter and the posterior thalamic region or the FEF and underlying structures. Ipsidirectional pursuit defects have also been recorded in patients with lesions in the midbrain tegmentum and basis pontis, the former deficits likely resulted from disruption of descending corticopontine connections, while the latter resulted from damage to the pontine nuclei themselves.

### TABLE 2

**CAUSES OF SYMMETRIC PURSUIT IMPAIRMENT**

- diffuse or multifocal cerebral damage
- Alzheimer's disease
- HIV-associated dementia
- cerebellar dysfunction
- Parkinson's disease
- Huntington's disease
- progressive supranuclear palsy
- schizophrenia
- affective disorders
- sedative-hypnotic medications
- anticonvulsants
- inattention
- fatigue
- senescence

In contrast to the ipsidirectional pursuit deficits associated with lesions of the cerebral hemisphere and rostral brainstem, caudal brainstem damage generally causes greater impairment of contralateral pursuit. Lateral medullary infarction reduces contralateral smooth pursuit velocities more than ipsilateral velocities. Caudal pontine tegmental damage may affect the paramedian pontine reticular formation (PPRF), causing paresis of conjugate eye movements toward the side of damage. The eyes often cannot be driven across the orbital midline with saccades, pursuit or the VOR, but, when pursuit is tested within the intact contralateral hemirange of movement, contralaterally-direct pursuit is worse. PPRF neurons do not participate in smooth pursuit or the VOR; patients with small, localized PPRF lesions may have severely impaired saccades but intact smooth pursuit. Contralateral pursuit defects in patients with unilateral pontomedullary damage probably result from disruption of excitatory vestibular nuclear efferents to the contralateral abducens nucleus. Occasional observations of ipsidirectional pursuit impairment in patients with lesions in this region might be explained by dysfunction of inhibitory Purkinje cell projections to the vestibular nuclei. Some brainstem lesions that alter smooth pursuit might do so by creating a tonic vestibular bias associated with nystagmus, as do peripheral vestibular lesions. Acute peripheral vestibular damage causes ocular drift toward the damaged side; ipsilateral smooth pursuit has higher velocities than contralateral pursuit. Pursuit asymmetry may persist for several weeks after peripheral vestibular lesions, even when primary position nystagmus is noted only in darkness.

Lateralized cerebellar dysfunction from extrinsic compression typically causes lower ipsilateral pursuit gain in patients, probably from involvement of the flocculus. Infarction of the caudal vermis and paraflocculus has been associated with impaired smooth pursuit in patients; both ipsidirectional and contralateral deficits have been reported. This difference may result from variable involvement of the region around the fastigial nucleus. Unilateral infarction of the rostral cerebellum reduces pursuit gain symmetrically in both horizontal directions.

### TABLE 3

**LOCALIZATION OF ASYMMETRIC SMOOTH PURSUIT DEFECTS**

**Ipsilateral directional deficits**
- MT/MST homologue
- frontal eye fields
- posterior thalamus/internal capsule
- midbrain/rostral pontine tegmentum
- basis pontis
- cerebellar flocculus

**Contralateral directional deficits**
- caudal pontine tegmentum
- lateral medulla
- caudal cerebellum
- acute peripheral vestibulopathy

**Selective vertical pursuit deficits**
- pretectum/dorsal midbrain

**Contralateral retinotopic deficits**
- geniculocalcarine pathway
- MT/MST homologue

**Contralateral craniotopic deficits**
- posterior parietal lobe
- frontal lobe
Damage in the pontomedullary tegmentum causes impairment of vertical pursuit, usually associated with other ocular motor deficits.\textsuperscript{25,31,52,75} Patients with internuclear ophthalmoplegia have only mild impairment of vertical smooth pursuit, suggesting that pathways outside the MLF carry most vertical pursuit commands in humans.\textsuperscript{55} Unilateral pretectal damage that includes the INC or the rostral interstitial nucleus of the MLF selectively impairs vertical eye movements, including smooth pursuit.\textsuperscript{10,55} Compression of the posterior commissure by pineal tumors limits the range of upward smooth pursuit.\textsuperscript{5}

At early levels of its organization (see Figure 4), the smooth pursuit system operates in terms of the retinal location of stimuli, with each cerebral hemisphere controlling motion processing in the contralateral visual hemifield. Patients with hemianopia due to lesions in the geniculocalcarine pathway do not track images normally when they are projected into their defective visual hemifield.\textsuperscript{45} Unlike directional pursuit defects, retinotopic defects like this can be reliably identified only in the laboratory with the use of step-ramp stimuli. Patients with hemianopia can track predictably oscillating targets like sinusoids quite smoothly by keeping the image over the seeing portion of the fovea and perifoveal retina.\textsuperscript{43,45,60} Patients with damage restricted to the MT/MST homologue may have selective defects of pursuit in the contralateral hemifield, without visual field loss on perimetry.\textsuperscript{45,70} This corresponds to a selective deficit for motion vision, a "motion hemianopia", which can also be demonstrated with psychophysical testing.\textsuperscript{7,90}

Patients with acute unilateral hemispheric damage and ipsilateral gaze deviation are often unable to make saccades or smooth pursuit across the orbital mid-position away from the side of damage.\textsuperscript{5,49,58} This deficit is a head-centered, or craniotopic, eye movement disorder, since it depends on eye position relative to the orbit. In these patients, smooth pursuit within the intact hemifield of eye movement is actually better in the direction away from the lesion than toward the lesion, demonstrating a superimposed ipsidirectional deficit.\textsuperscript{49} Patients with acute cerebral infarction, but without gaze deviation, may demonstrate milder forms of craniotopic pursuit impairment. In these patients, smooth pursuit can be generated to both the right and left of the orbital midline, but pursuit is worse in the hemifield of eye movement contralateral to the lesion. This type of eye movement deficit has been associated with damage to the frontal and posterior parietal lobes.

Most forms of acquired nystagmus result from imbalance of tonic eye movement pathways associated with the regulation of the VOR. However, abnormalities of the smooth pursuit system account for a few less common types of nystagmus. Patients with epileptogenic foci in the area of the MT/MST homologue may develop contralaterally-beating nystagmus during seizures.\textsuperscript{27} The ipsilaterally-directed slow phases of this nystagmus are thought to reflect activation of the smooth pursuit system. Patients with large, chronic cerebral hemispheric lesions may demonstrate low-frequency, non-paroxysmal nystagmus beating toward the injured hemisphere.\textsuperscript{43,62} These patients have marked reduction in smooth pursuit velocities toward the side of the lesion, while smooth pursuit away from the lesion can actually exceed target velocity. The ocular oscillation in these patients has been called pursuit-paretic nystagmus and attributed to the severe directional imbalance of smooth pursuit.

References
