Utrecht University

Sharing science,
shaping tomorrow

This is the author accepted manuscript (AAM) of the following published article:

Pupillometry as an integrated readout of distinct attentional networks

Christoph Strauch[1*], Chin-An Wang[2,3], Wolfgang Einhäuser[4], Stefan Van der Stigchel[1], and Marnix Naber[1]

[1]Experimental Psychology, Helmholtz Institute, Utrecht University, The Netherlands

[2]Institute of Cognitive Neuroscience, National Central University, Taoyuan City, Taiwan

[3]Cognitive Intelligence and Precision Healthcare Center, National Central University, Taoyuan City, Taiwan

[4]Physics of Cognition Group, Chemnitz University of Technology, Chemnitz, Germany

Affiliation

*Correspondence: c.strauch@uu.nl (C. Strauch).

Abstract

The course of pupillary constriction and dilation provides an easy to access, inexpensive, and non-invasive readout of brain activity. Here, we propose a new taxonomy of factors affecting the pupil and link these to associated neural underpinnings in an ascending hierarchy. Besides two well established low-level factors (light level and focal distance), we further suggest two intermediate-level factors, alerting and orienting, and a higher-level factor, executive functioning. Alerting, orienting, and executive functioning – including their respective underlying neural circuitry - highly overlap with the three principal attentional networks, making pupil size an integrated readout of distinct states of attention. As a now widespread technique, pupillometry is ready to provide meaningful applications and constitutes a viable part of the psychophysiological toolbox.

Keywords: Orienting, alerting, executive function, locus coeruleus, superior colliculus

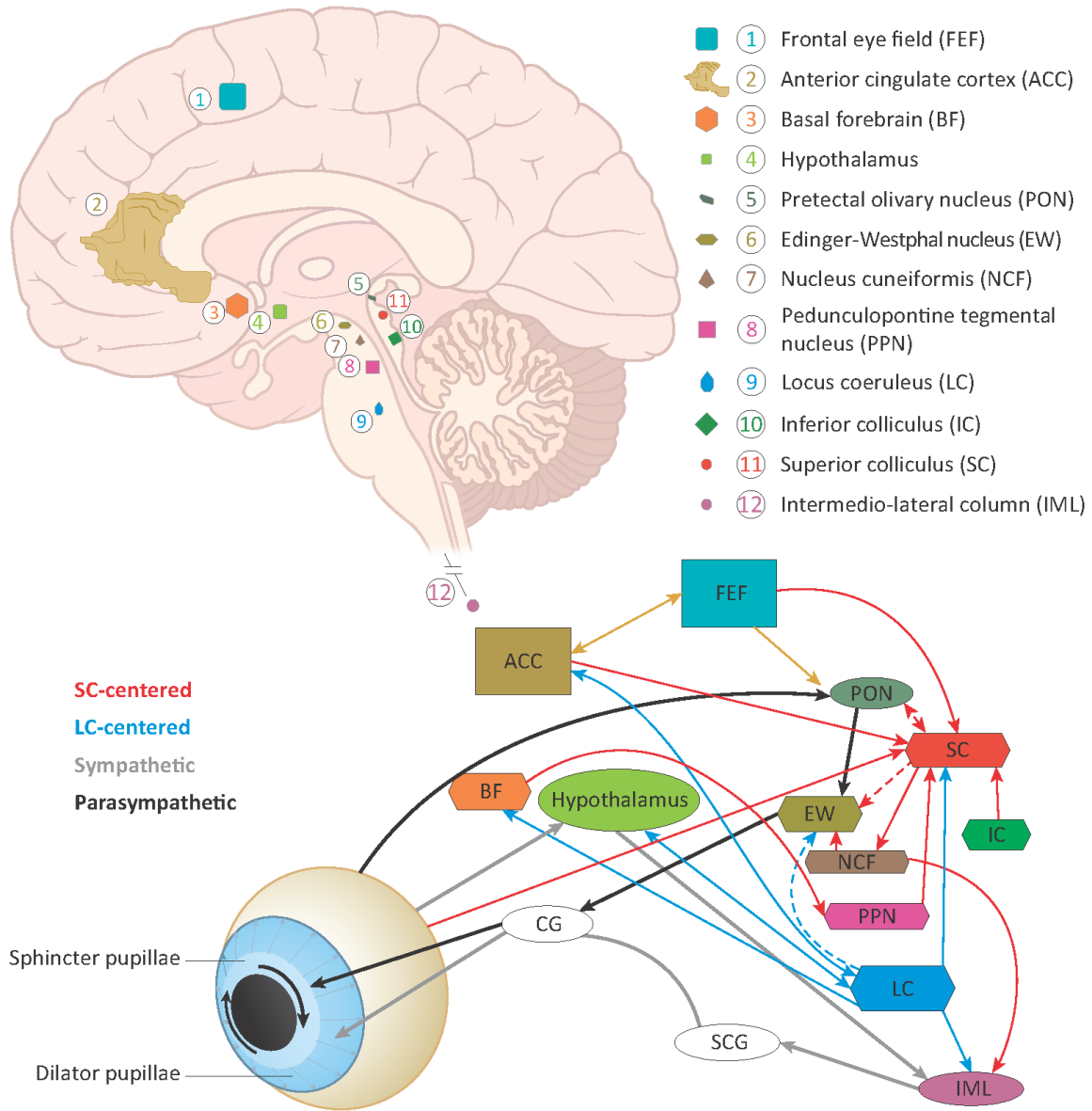1   **A new taxonomy of pupil responses**

2   The human pupil is a roughly circular aperture of variable size in the iris that allows light

3   to strike the retina. Pupil-size changes have been investigated as a neurophysiological

4   readout since the earliest days of psychology, neurology, ophthalmology, and neuroscience.

5   Well-documented effects in pupillometry span diverse factors, such as bodily and mental

6   effort, attentional shifts, or neurological diseases [1, 2]. Recent developments now allow us

7   to isolate more general, distinct types of pupil responses.

8   Here, we propose a novel taxonomy that divides pupil responses into five factors of low,

9   intermediate and higher levels of hierarchy and link intermediate and higher-level factors to

10   attentional functions. Low-level factors are **light level** and **focal distance** (when fixating

11   from far to near or vice versa). On the intermediate level rank **alerting** and **orienting**,

12   whereas **executive functioning** constitutes a higher-level factor. This distinction is

13   supported by evidence for four underlying neural circuits: Low-level **parasympathetic**

14   and **sympathetic** circuits yield all pupil responses via innervation of the pupillary

15   muscles, and intermediate-level subcortical areas that control pupil size. We argue that

16   changes so far coined as arousal-related in fact result from two partially overlapping, but

17   distinct neural circuits that are part of an overarching attention network on the

18   intermediate level: a **locus coeruleus (LC)-centered** circuit that brings about

19   alertness-related changes in pupil dilation and a **superior colliculus (SC)-centered**

20   circuit that mediates the pupil orienting response [3, 4]. These networks in turn receive

21   input from both sensory and executive control areas, the highest level in the proposed

22   hierarchy. These factors affect pupil size via a cascade adhering to the neural hierarchy: All

23   factors affect low-level parasympathetic and sympathetic circuits, intermediate-level factors

24   involve the intermediate LC-centered or SC-centered networks, and higher-level factors

25   involve circuits on all levels. The intermediate- and higher-level circuits and responses

26   largely overlap with factors and structures described in Petersen and Posner's networks of

27   attention [5]: alerting, orienting, and executive function. This suggests the pupil to

28   constitute an integrated readout of differential states/networks of attention. We propose

29   that the orienting and alerting systems match the SC and LC networks, respectively, and

30   that the executive function network (or fronto-parietal attention network), including its

31   connections to sensory areas, accounts for the role of top-down, focal attention in shaping

32   primary pupillary responses.

33   We present recent findings on pupillary dynamics following the aforementioned

34   taxonomy, including a brief overview of the associated neural underpinnings. We also

35   discuss some key experimental protocols, and highlight applications that emerged out of

36   more than a hundred years of pupillometry research. Circuits and involved areas are

37   visualized in Figure 1. The intermediate circuits are presented in more detail in Box 1.

38   Lastly, we provide an overview of techniques that may allow for dissociating the networks

39   introduced here, outline best practices in pupillometry research (Box 2), describe

40   pupillometry in relation to other psychophysiological measurements (Box 3), and highlight

41   applications of the five factors that drive pupil responses (Box 4).

Legend:
1. Frontal eye field (FEF)
2. Anterior cingulate cortex (ACC)
3. Basal forebrain (BF)
4. Hypothalamus
5. Pretectal olivary nucleus (PON)
6. Edinger-Westphal nucleus (EW)
7. Nucleus cuneiformis (NCF)
8. Pedunculopontine tegmental nucleus (PPN)
9. Locus coeruleus (LC)
10. Inferior colliculus (IC)
11. Superior colliculus (SC)
12. Intermedio-lateral column (IML)

SC-centered
LC-centered
Sympathetic
Parasympathetic

Sphincter pupillae
Dilator pupillae

Figure 1.

Pupillary dynamics

Pupillary dynamics can best be categorized into (1) steady-state changes in baseline pupil size and (2) transient changes relative to baseline pupil size [3]. Whereas the light level and focal distance only affect the pupil's steady-state, and orienting only evokes temporary changes, alerting and executive-control modulate steady-state *and* temporary changes in pupil size depending on whether sustained or transient state changes occur, respectively. Of the five proposed factors driving pupil size, two can be described as low-level, causing the pupil light response (PLR) and the pupil near response (PNR), while two

52   intermediate-level factors are linked to fluctuations in alerting and orienting. Lastly,

53   higher-level responses come into place due to executive function, including the interaction

54   between the control of focal attention and sensory processing. We next introduce the five

55   factors, from low-level to higher-level, along with recently emerged applications. We also

56   link the factors to the four circuits visualized in Figure 1.

Low-level responses

58   *Light levels*

59   First and foremost, a high retinal light level is associated with a constricted pupil state

60   whereas low retinal light level is associated with a relatively dilated pupil state.

61   Correspondingly, changes in retinal light levels let pupils dilate and constrict respectively,

62   likely as a relatively fast adaptation mechanism to improve contrast perception. In terms of

63   time course, pupil constrictions in response to a light level increase at the retina reach

64   minimum pupil size typically faster than 1 s and within 2 s maximum, while redilations

65   usually take several seconds, and can even take minutes after strong stimulation with blue

66   light [6]. Pupil response onset latencies are faster for constrictions (ranging from 200 ms to

67   400 ms) than for dilations, but these vary hugely as they depend on the individual and on

68   stimulus intensity [2, 6, 7].

69   The pupil light response and the neural structures mediating it are well-established [2].

70   Transient changes in steady-state pupil size in response to an increase or decrease in light

71   levels are mediated mainly by the activation of the parasympathetic or sympathetic

72   pathway, respectively [2]. As illustrated in Figure 1, many structures are involved in the

73   control of pupil size (see [2, 3, 8] for reviews). Briefly, the pupil is controlled by the

74   sphincter pupillae muscle (for constriction) and the dilator pupillae muscle (for dilation)

75   of the iris. These two muscles are mediated, respectively, by the parasympathetic (black

76   lines in Figure 1) and sympathetic (gray lines) pathways of the autonomic nervous system;

77   pupil size is hence determined by balanced activity between these two antagonistic

78   pathways. In the parasympathetic pathway, neurons in the Edinger-Westphal preganglionic

79   cell group (EWpg) project to the ciliary ganglion [9]. The cholinergic postganglionic

80   fibers in the ciliary ganglion target the muscles of the sphincter pupillae via the short

81   ciliary nerves.

82   The Edinger-Westphal (EW) nucleus receives projections from the pretectal olivary

83   nucleus (PON), and neurons in the PON receive direct retinal signals including ones

84   from intrinsically photosensitive retinal ganglion cells that are important for reflexive,

85   steady-state pupillary adaptations to daylight. In the sympathetic pathway, the

86   hypothalamus receives direct retinal input and projects to the ciliospinal centre located in

87   the intermediolateral cell column of the spinal cord (IML) at the level of C8–T2, though

88   the projections from the hypothalamus to the IML are less established. The preganglionic

89   neurons of the IML project to the superior cervical ganglia (SCG), and the adrenergic

90   postganglionic neurons of the SCG terminate in the dilator pupillae muscle via the long

91   and short ciliary nerves.

92   *Focal distance*

93   Steady-state pupil size is modulated by the focal distance, that is, the depth at which

94   both eyes fixate [10]. When fixation focus changes from far to near, the lens

95   accommodates, the eyes converge, and pupils constrict. These three aspects form what is

96   known as the near triad [2, 11]. Shortly after the lens is accommodated, the pupil starts

97   constricting. This constriction typically slightly overshoots, and the pupil starts to

98   redilate when accommodation is still maintained. Such a pupil constriction, like a

99   narrowing of the aperture of a camera lens, increases the depth of focus (or field),

100   meaning that objects slightly deviating in depth from the optimal fixation remain in focus.

101   When focus changes from near to far, the lens disaccommodates, the eyes diverge, and

102   the pupil dilates [11].

103   The pupil near-response is regulated by the parasympathetic pathway [11]. As pupil

104   constriction during near viewing is not correlated to responses in PON luminance neurons,

105   it is believed that the PNR is simply controlled by the EWpg [12]. A number of brain areas

106   are involved in the near triad, and the current model suggests that the PNR is driven by

107   an interaction of the accommodation and convergence controller [13].

108   **Intermediate-level responses**

109   *Alerting*

110   Vigilance and performance are related to arousal in an inverted-U shape. Optimal

111   performance is therefore generally observed at intermediate levels of arousal indicated by

112   pupil size [14]. As a modification of Petersen and Posner's broader term of *alerting* [5], it is

113   specifically the *intensity* of attention [15] that seems to be most closely reflected in pupil

114   size. Whereas steady oscillations in pupil size around baseline reflect fatigue [16],

115   steady-state pupil size is determined by general arousal levels [17, 18]. Temporary

116   responses reflect short-lasting deviations from baseline, characterized as sudden dilations or

117   constrictions in response to changes in internal mental states. Internal events that dilate

118   pupils include factors such as evidence accumulation during decision-making, processing of

119   self-relevant, emotional, or sexual stimuli and are commonly traced back to changes in

120   mental effort [19] [see 20, 21, for reviews], in other words to changes in the intensity of

121   attention. The intensity of attention in turn relates to many higher-level processes, which

122   is part of the reason why so many higher-level factors are reflected in pupil size.

123   Furthermore, movement or its preparation, for instance pressing a key, causes a pupil dilation

124   that likely only partially reflects the foregoing decision [22, 23, 24].

125   Differential roles of tonic and phasic LC-activity, reflected in distinct pupil dynamics, have

126   been suggested as part of the influential adaptive-gain theory [25]. The theory relates to

127   concepts from the foraging behavior field, which differentiates between period of

128   exploitation (consuming resources) and exploration (seeking for new resources). According

129   to the adaptive-gain theory, during periods of exploitation, task-engagement is maintained,

130   distraction is shielded against, and information is processed accurately. In these periods,

131   baseline firing rate of the LC is moderate and baseline pupil size remains small. In

132   response to relevant events, phasic firing of the LC occurs and results in transient pupil

133   dilations. During (tonic) periods of exploration, task-disengagement and the exploration

134   of new sources of reward is facilitated and baseline firing of the LC and pupil size is

135   elevated [26, 27, 28]. This contrast concurs with the rest-and-digest versus fight-flight

136   function of the parasympathetic versus sympathetic components of the autonomous,

137   peripheral nervous systems, respectively [2, 29]. The adaptive gain theory therefore links

138   phasic and tonic components driving pupil size changes to behavior across different

139   species [30, 31, 32, 33, 34]. Modeling accounts allow to understand functional roles of

140   pupil responses in task behavior, and such modeling suggested for instance differential

141   roles of phasic responses linked to stimulus encoding and of decision formation in mice

142   [33].

143   The alerting **LC-centered circuit** releases norepinephrine and connects to most of the

144   brain (see Box 1 for a detailed description and Figure 1 for a visualization). This is

145   demonstrated, among other ways, by conjoint fMRI and pupillometry investigations,

146   showing a high degree of covariation between changes in pupil size and LC-activation

147   [35, 36] and by animal studies in which microstimulation of the LC results in pupil-size

148   changes [37, 38, 39]. A crucial role of input from the orbitofrontal cortex (OFC) and

149   anterior cingulate cortex (ACC) to the LC has been proposed as part of the adaptive-gain

150   theory, with the OFC being linked to evaluating reward and the ACC being linked to

151   evaluating cost [25]. While innervations of the LC by the ACC are established in

152   multiple species, such innervations by the OFC are found in rodents but not primates

153   [40, 41, 42], requiring further investigation.

154

155   *Orienting*

156   The appearance of an external, salient, and relatively novel stimulus in the environment

157   initiates a repertoire of orienting responses to prepare the body for possible action for

158   survival, including attentional shifts, eye/head/body movements, and changes in pupil size

159   [43, 44]. Temporary pupil responses following attentional re-orienting may occur in

160   isolation, but are mostly observed in parallel with steady-state changes in pupil size caused

161   by alterations in light levels, focal distance, or alertness that stimulus onsets typically also

162   evoke (e.g., see [45]). However, due to differences in latency, pupil orienting responses

163   slightly precede responses linked to alerting and the pupil dark response. Multiple

164   components within a pupil response (e.g., a dilation to a decrease in light levels

165   superimposed on a constriction after re-orienting) can be disentangled using

166   (de)convolution modelling [46] if the implementation of control conditions is not feasible.

167   Pupillary orienting responses are by definition short-lasting. The pupil changes (most often:

168   constricts) in response to any type of visual event, even when the global luminance level

169   remains unaltered, whether it is a change in local or global contrast [47, 48], color [48, 49],

170   spatial frequency [50], orientation [51], motion velocity [49], or (apparent) motion direction

171   [52, 53, 54]. Moreover, these pupillary orienting responses are evoked independent of

172   stimulus modality [55, 56, 57], and enhanced by multisensory presentation in an additive and

173   linear manner [23, 24]. More importantly, the speed and amplitude of evoked pupillary

174   orienting responses scale with salience [55, 58, 59], suggesting that this response is indeed

175   linked to orienting. Interestingly, the amplitude of such saliency-driven responses is shaped

176   by the depth of sensory processing, such as the degree of attention and awareness for the

177   external events (for reviews, see [60, 61]). So far, it remains unknown why the pupil

178   orienting response consists of a constriction or dilation depending on the type of stimulus

179   being used. As the orienting response is spatial in nature, it can even reveal biases in spatial

180   attention (e.g., "pseudoneglect") [62]. The generalization of effects of pupillary modulation

181   in response to stimuli across sensory domains suggests the existence of an underlying

182   modality-independent orienting system. This system is likely mediated by the SC-centered

183   circuit (see Box 1), which receives multisensory [63] and cognitive signals from many areas

184   such as the Frontal Eye Field (FEF) and basal ganglia [4]. Thus, pupil-size changes likely

185   reflect attentional orienting in response to a novel stimulus and reflect a process serving

186   the ability to prioritize sensory input by its modality or location [5].

187   As highlighted in Box 1 and visualized in Figure 1, the SC forms the hub of a network

188   underlying pupil responses related to the integration of multisensory input and prominent

189   areas in the orienting-network by Petersen and Posner [5], such as the FEF and ACC [64].

190   Thus, activity best described as orienting response affects the size of the pupil. The SC-

191   centered circuit which we have outlined here is proposed to be the primary network

192   underlying the pupil orienting response, the speed of which is determined by the

193   LC-centered alerting circuit which provides direct input to the SC [65]. It should be

194   noted, however, that the response latency to sensory stimulus onset is shorter for SC [66]

195   than LC neurons [67], suggesting alertness at stimulus onset to be predictive of the speed

196   of the orienting response, whereas changes in alertness elicited by the same stimulus are

197   too late to affect the speed of that respective orienting response. In line with this notion,

198   pupil response onset latencies are shorter for microstimulation of the SC than the LC

199   [37], suggesting the SC to be closer to the final common path.

200

201   **Higher-level responses modulated by executive functions**

202   Higher-level factors that affect the pupil can be subsumed under the notions of sensory

203   interpretation and executive function, with the latter being the broadest of Petersen and

204   Posner's factors [5]. Executive functions, among other roles, allow to guide the allocation

205   of focal attention to control the depth of processing and degree of awareness of the most

206   relevant and novel targets in the environment. Attention can be endogenously directed

207   (top-down guided) to a target, which can consist of either a spatial element (e.g., a visual

208   location), a physical entity (e.g., a person), or a specific feature (e.g., the pitch of a voice

209   within a conversation at a cocktail party). When focal attention is allocated to a target, it

210   is processed in depth - at the expense of other items - enabling more efficient processing.

211   Such effects of attention operate, in part, on early sensory representations, enhancing

212   targets relative to distractors. It is therefore perhaps no surprise that

213   higher-level cognitive functions leave a mark on pupillary dynamics in a manner reflecting

214   sensory operations [see 60, 61, 68, for reviews].

215   The strongest evidence of how higher-level cognitive processes shape pupil size comes from

216   studies that manipulate perception (i.e., the content of awareness) despite a constant

217   physical stimulation. Using bi-stable (ambiguous) figures that evoke alternating dark or

218   bright percepts depending on the observer's subjective state, pupil size will increase when a

219   dark percept is dominant and decrease when a bright percept is dominant, even though the

220   stimulus itself does not change [52, 69]. Furthermore, studies on mental imagery, a

221   higher-level cognitive operation, showed that mentally visualizing a dark scene leads to a

222   pupil dilation [70], and natural scene studies showed that the presentation of illusory bright

223   stimuli, like images of a sun, evokes pupil constrictions [68, 71, 72, 73]. Similarly, the

224   interpretation of a scene as close in depth has recently been associated with a pupil

225   constriction compared with the interpretation as far [74], as is the mental imagery of close

226   compared with distant objects [75] via the pupil-near response.

227   The aforementioned phenomena can be exploited to discern which objects or parts of a

228   scene are attended [76] or how spatial attention is deployed [62, 77].When separate objects

229   (or visual field regions) are tagged with a distinct light level, the attended object's

230   luminance but not its surrounding determines pupil size [60, 61, 72, 78]. Objects can also

231   be tagged with distinct luminance flicker frequencies (or phases), accordingly affecting the

232   pupil in a manner that allows the on-line identification of which objects are attended or

233   ignored [76, 79].

234   Besides such higher-level effects on steady-state adaptations of pupil size to subjective

235   brightness and depth perception, executive functions similarly affect the pupil's orienting

236   responses. The degree to which a stimulus receives attention determines the pupil

237   responsiveness, and this applies to onsets of both auditory [80, 81, 82] and visual stimuli

238   [76, 83]. The degree of pupil responsiveness during orienting may similarly depend on the

239   saliency of subjective events, like the perceptual change of an ambiguous stimulus [45, 52,

240   84, 85, 86] or even the number of stimuli present in a display [87]. In a similar vein,

241   presentations of stimuli with preferred and common features tend to evoke stronger pupil

242   constrictions than stimuli displaying less preferred/common features. For example, the

243   presentation of sine-wave gratings at around 3 cycles per degree, a spatial frequency

244   preferred by the visual system, evokes stronger pupil constrictions than other spatial

245   frequencies [47, 50, 88]. Uncommonly processed stimuli, such as an inverted natural scene,

246   let the pupil constrict only weakly [73, 89]. When a novel rather than familiar stimulus is

247   shown, the pupil constricts more strongly [90, 91].

248   The cortical processing of stimuli follows a hierarchy, with changes in simple stimulus

249   features (e.g., contrast) evoking activity at early stages and changes in more complex

250   features (e.g., shape) at later stages. Orienting responses to stimuli reflect the timing of

251   these operations as the complexity of a stimulus positively correlates with pupil

252   constriction latencies [48]. Besides saliency (conspicuity), pupil responses thus also depend

253   on the timing of the onset of processing of sensory events. The pupil as a tool to mark the

254   order of processes has been demonstrated beyond sensory tasks, including the highlighting

255   of object detection versus subsequent identification phases [92] and ballistic versus

256   subsequent error-correction phases of motor coordination [27].

257   The attention network subserving executive function consists of frontal and parietal

258   regions. Frontal regions include the dorsolateral prefrontal cortex (DLPFC), FEF, ACC, as

259   well as pre-motor cortex, and are mostly responsible for initiating changes in focal

260   attention. Parietal regions include the temporal-parietal junction (TPC), intraparietal

261   sulcus and adjacent areas (e.g., LIP), and several other regions implicated in integrating

262   visuomotor information to shift attention covertly (without eye movements) or overtly

263   (with eye-movements). These latter areas reciprocally connect to sensory regions to

264   enhance target processing and to plan subsequent shifts to novel targets, including

265   through the feedback of information to frontal regions. Frontal regions, particularly the

266   FEF and ACC, likely modulate the aforementioned higher-level effects on pupil size

267   through the close connection to the SCi [44]. The topographic organization of the SC, in

268   particular, marks this neural locus as a likely candidate to mediate pupillary effects of

269   covert spatial attention to stimulus events (enhanced orienting) and anisotropies in

270   background light levels (enhanced light response) [93].

271   It should be noted that the FEF also directly projects to the visual cortex [94] and the

272   PON [95], potentially modulating sensory regions and changes in pupil size, but this

273   proposition remains to be established. Additionally, the LC connects to the ACC and

274   OFC anatomically and functionally, a pathway which is also involved in pupil size control

275   and important to executive function [5, 96, 97]. Thus, the LC-centered circuit can also

276   mediate higher-level pupillary responses. As the LC is non-topographically organized,

277   we argue that the LC provides critical control signals to topographically sensitive structures

278   [93], particularly the SC, to coordinate movements that are spatially directed (e.g.,

279   saccades) or non-spatially directed (e.g., pupil responses).

280

Concluding remarks and future perspectives

282   Pupil size is influenced by a wide variety of factors, which we categorize into low-level

283   factors – **light-level** and **focal distance;** intermediate-level factors – **alerting** and

284   **orienting;** and higher-level phenomena, subsumed under **executive function**. Neural

285   circuits underlying low-level, intermediate-level, and higher-level effects interactively

286   change pupil size in a cascaded manner. As low-level and principal circuits, the

287   parasympathetic and the sympathetic pathways control pupil responses from all levels of

288   the hierarchy. The LC-centered and the SC-centered circuits underlie intermediate-level

289   pupil responses. Effects linked to higher-level executive function are likely mediated via

290   the LC- and SC-centered circuits, in which the ACC and FEF are particularly involved.

291   Because the LC and SC have extensive connections to many brain regions (beyond the

292   ACC and FEF), future research is required to explore their connections to these structures

293   that may also contribute to higher-level pupil modulations.

294   The intermediate and higher-level factors affecting pupil size, as well as their associated

295   networks overlap with the attentional networks introduced by Petersen and Posner [5],

296   suggesting that the pupil provides an integrated readout of activity in each attentional

297   network. With the proposed taxonomy, we seek to demonstrate the rich neurophysiological

298   signal that the timecourse of pupillary constriction and dilation provides and to outline

299   further avenues for advancing its understanding. Many intriguing questions remain to be

300   addressed in future work (see Outstanding Questions). For instance, future research will

301   have to further elucidate the existence of differential factors within executive function,

302   possibly by identifying differential components in the pupillary signal. At the level of

303   neural circuitry, the (causal) identification of distinct and clearly defined circuits

304   bringing about changes in relation to executive function could further help isolate these

305   possible subcomponents of executive function. Furthermore, the relation between pupil-size

306   changes and other peripheral indicators is still not fully understood, and it is likely that the

307   pupil differs from other psychophysiological indicators in more than just sensitivity. Yet,

308   a deepened understanding of these relationships may allow for the isolation of much more

309   specific cognitive factors by combining peripheral indicators of arousal that are sensitive

310   to differential factors. Furthermore, such measurement combinations could bring about

311   robust applications by factoring out effects of individual factors that selectively affect one

312   but not all indicators obtained simultaneously.

313

314 **Box 1. Neural circuitry involving the locus coeruleus, superior colliculus, and**

315 **basal forebrain.**

316 The **locus coeruleus (LC)-centered circuit** mediates pupil responses related to alterations

317 in the arousal system mainly via releasing norepinephrine throughout most of the brain

318 [3, 25]. In behaving monkey, baseline (steady-state) pupil size during passive fixation and

319 temporary pupil responses evoked by acoustic stimuli or stimuli related to effort and reward

320 positively correlate with LC activity [37, 98]. Similarly, in humans performing cognitive tasks,

321 LC BOLD activity positively correlates with pupil size [35] and responses [36]. Moreover, LC

322 microstimulation in monkeys and rats evokes pupil dilation [37, 38], and pupil dilations are

323 also observed after LC-NE activity in the cortex of awake mice [39, 99], although these

324 correlations vary considerably over time [100]. While the latter finding warns against

325 interpreting pupil size as direct readout of LC activity, notably, latencies in primates are

326 fundamentally different than those in rats [37, 38]. It is hypothesized that LC efferent

327 projections to the IML and hypothalamus could underlie coupling between pupil size and

328 LC activity [3].

329 The **superior colliculus (SC)-centered circuit** mediates the orienting pupil response [4].

330 The intermediate SC (SCi) integrates multisensory, arousal, and cognitive signals from

331 various areas including the superficial superior colliculus (SCs), inferior colliculus (IC), LC,

332 lateral intraparietal cortex (LIP), anterior cingulate cortex (ACC) and frontal eye fields

333 (FEF), and projects directly to the brainstem premotor circuit to coordinate the orienting

334 response including eye/head/body movement, attention shifts, and pupil responses [44, 101].

335 SCi microstimulation can evoke pupil dilation [37, 102, 103], with similar dilation observed

336 following IC, LC, and FEF microstimulation [37, 104]. The SCi, compared to the LC and

337 IC, has the shortest microstimulation-evoked pupil response onset latency [37], suggesting

338 that the SCi is the structure that is most closely located to the final common path. Besides,

339 the SCi and FEF are causally involved in alternating pupil size as a function of the focus

340 of attentional switches between locations with varying luminance [93, 105], explaining pupil

341 brightness responses induced by higher-level cognition [60, 61]. The SCi connects to the

342 EW nucleus mostly indirectly via the central mesencephalic reticular formation (cMRF; or

nucleus cuneiformis in humans) [106, 107]. The EW nucleus projects to the ciliary ganglion with excitatory and inhibitory connections [108], which at least theoretically could produce both constriction and dilation. The SC also links to the medullary reticular formation directly and indirectly via the cMRF to possibly influence preganglionic sympathetic motoneurons [109], together providing the necessary connections to change pupil size.

Cholinergic neurons of **the basal forebrain (BF)** are activated during pupil dilation in walking mice [39, 110]. LC projections to the BF could underlie these pupil correlations [3]. Notably, the cholinergic BF functionally connects to the pedunculopontine tegmental nucleus (PPN), as injection of inhibitory lidocaine in the BF causes reduced activation elicited by PPN stimulation [111]. The SCi receives PPN projections, and changing SC cholinergic activity via PPT input modulates saccade responses [112]. Together, the BF could be involved in pupil modulations related to alerting and orienting.

As pupil size is modulated by neural activity from noradrenergic brainstem nuclei (e.g., LC), the orienting circuit (e.g., SC), and cholinergic BF, we argue that all these circuits are involved in modulating pupil size during executive functioning.

Box 2. Pupil size as part of the psychophysiological toolbox.

Whereas both the parasympathetic and the sympathetic branch of the autonomous nervous system control pupil size, two other popular psychophysiological indicators, **heart rate** and **skin conductance,** are predominantly controlled by the former [113] and latter [114], respectively. To what extent and for which tasks the pupil provides independent information relative to these measures and to the **EEG** (power in certain frequency bands or components of the event-related potentials (ERPs) [115]) is therefore of particular interest.

Correlations between pupil, heart rate and skin conductance have been reported, for example when viewing emotionally charged pictures, and suggest a common underlying system [80]. In contrast to arousal, valence seems to only affect heart rate, but not skin conductance and pupil size [116]. Skin conductance and heart rate can each predict unique components of the variations in pupil size, even on a trial-by-trail basis, suggesting that the pupil provides combined information from the sympathetic and parasympathetic systems [117]. Studies manipulating expectancy have shown that all three peripheral physiological measures relate to task preparation, but exhibit little between-subject or trial-by-trial correlations [118]. Similarly, mental fatigue affects heart rate variability, but leaves EEG, skin conductance, and pupil responses largely unaffected, whereas they scale similarly with reward [119]. During resting state, pupil size and skin conductance correlate [120], but in fear conditioning they clearly capture distinct aspects [121, 122]. In line with the latter, in rats, unique information is provided by both heart rate and pupil size on behavioral performance [123]. In EEG, the P3 ERP component shows similarities with phasic pupil dilations, for instance for time-on-task effects, but a mere alertness/LC-account is insufficient to explain all relations between these measures [17].

In sum - depending on the paradigm - **pupil size, skin conductance, heart rate and EEG-based measures are related** [see 124, for a review], **but often capture distinct aspects of underlying processes and their respective circuitry**. Unlike EEG, peripheral measures, in particular pupil size, are one-dimensional and no spatial dimension is available. Unlike the general ERP, the pupil reflects activity in the highly specified subset of subcortical regions outlined in Figure 1. This might be one of the reasons why less trials are usually needed in

389   pupillometry compared to EEG research. Nonetheless, advanced data-analysis techniques
390   put forward for EEG can be useful in pupillometry (see Box 3). Such techniques might
391   eventually reveal more subtle relations between the indicators than simple correlations
392   between more or less raw signals. While EEG can extract physiologically meaningful signals
393   up to the high gamma range (around 60 Hz), pupillometry is limited by the frequency response
394   of the pupil (up to about 3 Hz [76]) with the other measures even slower. Associated
395   latencies and their variability thus limit the throughput of experimental paradigms. To this
396   end, pupillometry often provides a good compromise between the speed of EEG and the
397   relative simplicity and robustness of measurement of peripheral psychophysiological signals.

398

Box 3. Best practices in pupillometry research. Any stimulus used to study intermediate- or higher-level effects needs to be equalized for luminance, contrast, and other feature distributions across space. **Brightness**, **movements**, such as button presses [22, 23, 24], as well as other factors outlined in text must be kept constant or controlled for, unless being a manipulation of interest. For instance, even the tiniest luminance difference, such as the amount of eye-white (sclera) visible in face stimuli [125] or slight local differences in brightness [126] can already confound pupillary responses. Similarly, **stimulus location**, including stimuli presented (1) in the periphery, (2) monocularly near the nose (nasal), or (3) achromatically in the lower visual field evoke weaker pupil responses than other locations [127]. **Blinks** often induce a pupil constriction and are followed by a later redilation [57, 128]. Blinks can be treated as missing data or be interpolated, the latter being more useful in context of analyses over time points. **Saccades** (planning and execution) may cause either pupil dilations or constrictions [57, 129]. **Gaze position** changes distort the estimated pupil size depending on the angle of video-based eye-trackers, but can be corrected for [130].

Latencies of pupillary responses are crucial for planning the duration of trials and inter-stimulus intervals. Based on the **linearly additive model** of pupil-size changes [e.g. 131] - at least in non-extreme ranges of baseline pupil size that can lead to **floor/ceiling effects** - the usage of subtractive rather than divisive **baselines** is usually advised for [132, 133]. Similarly, there is no standard for the **units of pupil size effects**. Absolute deviation (mm, pixels, arbitrary units) better represents the underlying model of the event-related pupil response than divisive units such as percentage changes or z-standardized values, although the latter offers the unique advantage of putting effects in context with variation directly and removes individual differences in pupil response sensitivities. Millimeters are generally best suited for reporting effects. Millimeters are understandable, more useful for practitioners who rely on anatomical size, allow to identify possible floor/ceiling effects and to compare effect sizes across studies. As for baselines and units, there is no established standard (besides recent attempts, see [134]) for **conducting and reporting statistics**, as well as for **correcting for multiple tests**. Amplitudes, maxima, or minima in pupil size may be reported, which can be more prone to noise than averages over intervals, which in turn are

428 prone to cherry-picking. In the absence of prior knowledge about 'pupil components'

429 (analogous to ERP components), we argue in favor of using time-point-wise analysis [86,

430 135] with the appropriate α-level correction. Based on a common practice for spatial

431 dependency in fMRI research [136], we recommend the usage of **cluster-based**

432 **corrections to avoid alpha error inflation**, as tests are locally highly dependent on

433 adjacent tests over time. Alternatively, a data-driven decomposition into components, for

434 instance with PCA, or weighted pulse event function modelling can be advisable [46, 56,

435 57, 83].

436

Box 4. Applications of pupil size measurements. As the pupil response can be accessed relatively easily by contact-free measurements, it offers a broad variety of applications. In **clinical diagnostics and research**, alterations of the pupil may indicate neurological damages, arguably one of the oldest pupillometry applications. Today, ample evidence exists on distinctions between healthy controls and individuals with conditions ranging from schizophrenia, autism spectrum disorder [137] (but see [138]), anxiety and phobia, Parkinson's disease, and Alzheimer's disease (see [7, 20] for reviews).

In **ophthalmology**, pupil perimetry can detect visual field impairments, whether caused by retinal damage as a consequence of glaucoma, other eye diseases, or cerebral visual impairments [139, 140]. Here, pupil changes are visually evoked to assess awareness of (or visual sensitivity to) stimuli across the visual field [140, 141]. Stimuli presented in a patient's scotoma let the pupil constrict with about half of the amplitude of healthy controls [142]. Similarly, attentional spatial biases, such as present in hemispatial neglect, can be revealed using pupillometry [62]. **Pupil-computer interfaces (PCI)** exploit pupillometry for a user to signal information actively (e.g., to input text, intended particularly for patient populations) or passively (e.g., to adapt an interface to arousal levels). Voluntary shifts in focus from far-to-near and near-to-far and the resulting pupil responses allow users to communicate about six bits per minute [143]. The pupil can decode which of several differentially flickering targets is covertly attended [76], which allows text input at about par to the best steady-state evoked potential-based brain computer interfaces [78]. As the pupil indicates changes in mental effort, locked-in patients could communicate "yes" or "no" by performing mental arithmetic for the time interval in which the response was presented - without the need for training or individual adjustment [144]. Based on effects of changes in mental effort on pupil size during decision-making [23, 30], binary decisions can be decoded in up to 75% success rate and thus contribute to intent predictions in PCIs [145]. The tight coupling between alertness and pupil size has been used as input signal for **biofeedback** applications [146, 147]. Alertness-adaptive interfaces can use sensed information, e.g., to adjust video gameplay dynamics [148].

The **continuous monitoring of mental effort or workload** via pupillometry is a popular

466   suggestion for many applied domains ranging from education sciences to human-computer

467   interaction or human factors, e.g., in driving contexts [149]. While in many of the envisioned

468   settings, other relevant factors - like rapidly changing light levels - are hard to control, the

469   notion of measuring effort also allows screening **non-visual deficits** with pupillometry. For

470   instance, close-to-deaf listeners likely apply more mental effort to decipher what is heard,

471   resulting in pupil dilations [150, 151, 152].

472

Figure legend

Figure 1: **Schematic overview of pupil control pathways**. Top: Visualization of key pupil-associated structures in sagittal cut of the human brain. Numbers, colors, and symbolic shapes in the brain figure indicate structures that correspond to the legend on the right. Bottom: Four main neural circuits determine pupil size: The parasympathetic (black) and sympathetic (gray) paths as low-level circuits (oval shapes), LC-centered (blue), and SC-centered circuits (red), as intermediate-level circuits (hexagonal shapes), and connecting points to higher-level circuits, such as frontal eye-fields and ACC (rectangles). Solid lines denote established connections whereas dashed lines denote plausible, but less definitively established connections. Yellow projections are anatomical pathways that do not form part of the four circuits outlined here.

Declaration of interests

The authors declare no competing interests.

References

[1] Bumke, O. (1911). *Die pupillenstörungen bei geistes-und nervenkrankheiten [the pupil disorders in mental and nervous diseases]* (2nd ed.). Fischer.

[2] Loewenfeld, I. (1999). The pupil: Anatomy, physiology and clinical applications.

[3] Joshi, S., & Gold, J. I. (2020). Pupil size as a window on neural substrates of cognition. *Trends in cognitive sciences*, *24* (6), 466–480. https://doi.org/10.1016/j.tics.2020.03.005

[4] Wang, C.-A., & Munoz, D. P. (2015). A circuit for pupil orienting responses: Implications for cognitive modulation of pupil size. *Current opinion in neurobiology*, *33*, 134–140. https://doi.org/10.1016/j.conb.2015.03.018

[5] Petersen, S. E., & Posner, M. I. (2012). The attention system of the human brain: 20 years after. *Annual review of neuroscience*, *35*, 73–89. https://doi.org/10.1146/annurev-neuro-062111-150525

[6] Markwell, E. L., Feigl, B., & Zele, A. J. (2010). Intrinsically photosensitive melanopsin retinal ganglion cell contributions to the pupillary light reflex and circadian rhythm. *Clinical and Experimental Optometry*, *93* (3), 137–149. https://doi.org/10.1111/j.1444-0938.2010.00479.x

[7] Wilhelm, H. (2011). Disorders of the pupil. In C. R. Kennard & J. Leigh (Eds.), *Handbook of clinical neurology* (pp. 427–466). Elsevier. https://doi.org/10.1016/B978-0-444-52903-9.00022-4

[8] McDougal, D. H., & Gamlin, P. D. (2015). Autonomic control of the eye. *Comprehensive Physiology*, *5* (1), 439. https://doi.org/10.1002/cphy.c140014

[9] Kozicz, T., Bittencourt, J. C., May, P. J., Reiner, A., Gamlin, P. D., Palkovits, M., Horn, A. K., Toledo, C. A., & Ryabinin, A. E. (2011). The edinger-westphal nucleus: A historical, structural, and functional perspective on a dichotomous terminology. *Journal of Comparative Neurology*, *519* (8), 1413–1434. https://doi.org/10.1002/cne.22580

[10] Mays, L. E., & Gamlin, P. D. (1995). Neuronal circuitry controlling the near response. *Current opinion in neurobiology*, *5* (6), 763–768.

519   https://doi.org/10.1016/0959-4388(95)80104-9

520   [11]   Kasthurirangan, S., & Glasser, A. (2005). Characteristics of pupil responses during

521   far-to-near and near-to-far accommodation. *Ophthalmic and Physiological Optics*,

522   *25* (4), 328–339. https://doi.org/10.1111/j.1475-1313.2005.00293.x

523   [12]   Zhang, H., Clarke, R. J., & Gamlin, P. D. (1996). Behavior of luminance neurons in

524   the pretectal olivary nucleus during the pupillary near response. *Experimental brain*

525   *research.Experimentelle Hirnforschung.Experimentation cerebrale*, *112* (1), 158–162.

526   http://www.ncbi.nlm.nih.gov/pubmed/8951418

527   [13]   Myers, G. A., & Stark, L. (1990). Topology of the near response triad. *Ophthalmic*

528   *and Physiological Optics*, *10* (2). https://doi.org/10.1111/j.1475-1313.1990.tb00972.x

529   [14]   McGinley, M. J., Vinck, M., Reimer, J., Batista-Brito, R., Zagha, E.,

530   Cadwell, C. R., Tolias, A. S., Cardin, J. A., & McCormick, D. A. (2015). Waking

531   State: Rapid Variations Modulate Neural and Behavioral Responses. *Neuron*, *87* (6),

532   1143–61. https://doi.org/10.1016/j.neuron.2015.09.012

533   [15]   Just, M. A., & Carpenter, P. A. (1993). The intensity dimension of thought:

534   Pupillometric indices of sentence processing. *Canadian Journal of Experimental*

535   *Psychology/Revue canadienne de psychologie expérimentale*, *47* (2), 310.

536   https://doi.org/10.1037/h0078820

537   [16]   McLaren, J. W., Erie, J. C., & Brubaker, R. F. (1992). Computerized analysis of

538   pupillograms in studies of alertness. *Investigative ophthalmology & visual science*,

539   *33* (3), 671–676.

540   [17]   Murphy, P. R., Robertson, I. H., Balsters, J. H., & O'connell, R. G. (2011).

541   Pupillometry and p3 index the locus coeruleus–noradrenergic arousal function in

542   humans. *Psychophysiology*, *48* (11), 1532–1543.

543   https://doi.org/10.1111/j.1469-8986.2011.01226.x

544   [18]   Murphy, P. R., Vandekerckhove, J., & Nieuwenhuis, S. (2014). Pupil-linked arousal

545   determines variability in perceptual decision making. *PLoS computational biology*,

546   *10* (9), e1003854. https://doi.org/10.1371/journal.pcbi.1003854

547   [19]   Mathôt, S. (2018). Pupillometry: Psychology, physiology, and function. *Journal of*

548   *Cognition*, *1* (1). https://doi.org/10.5334/joc.18

549   [20] Einhäuser, W. (2017). The pupil as marker of cognitive processes. *Computational*

550   *and cognitive neuroscience of vision* (pp. 141–169). Springer.

551   https://doi.org/10.1007/978-981-10-0213-7_7

552   [21] Laeng, B., Sirois, S., & Gredebäck, G. (2012). Pupillometry: A window to the

553   preconscious? *Perspectives on psychological science*, *7* (1), 18–27.

554   https://doi.org/10.1177/1745691611427305

555   [22] Einhäuser, W., Koch, C., & Carter, O. L. (2010). Pupil dilation betrays the timing

556   of decisions. *Frontiers in Human Neuroscience*, *4*, 1–9.

557   https://doi.org/10.3389/fnhum.2010.00018

558   [23] Strauch, C., Koniakowsky, I., & Huckauf, A. (2020). Decision making and oddball

559   effects on pupil size: Evidence for a sequential process. *Journal of cognition*, *3* (1).

560   https://doi.org/10.5334/joc.96

561   [24] Van der Stoep, N., Van der Smagt, M., Notaro, C., Spock, Z., & Naber, M. (2021).

562   The additive nature of the human multisensory evoked pupil response. *Scientific*

563   *reports*, *11* (1), 1–12. https://doi.org/10.1038/s41598-020-80286-1

564   [25] Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus

565   coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annu.*

566   *Rev. Neurosci.*, *28*, 403–450.

567   https://doi.org/10.1146/annurev.neuro.28.061604.135709

568   [26] Jepma, M., & Nieuwenhuis, S. (2011). Pupil diameter predicts changes in the

569   exploration–exploitation trade-off: Evidence for the adaptive gain theory. *Journal of*

570   *cognitive neuroscience*, *23* (7), 1587–1596. https://doi.org/10.1162/jocn.2010.21548

571   [27] Naber, M., & Murphy, P. (2020). Pupillometric investigation into the

572   speed-accuracy trade-off in a visuo-motor aiming task. *Psychophysiology*, *57* (3),

573   e13499. https://doi.org/10.1111/psyp.13499

574   [28] Gilzenrat, M. S., Nieuwenhuis, S., Jepma, M., & Cohen, J. D. (2010). Pupil

575   diameter tracks changes in control state predicted by the adaptive gain theory of

576   locus coeruleus function. *Cognitive, Affective, & Behavioral Neuroscience*, *10* (2),

577 252–269. https://doi.org/10.3758/CABN.10.2.252

578 [29] Jänig, W., & Häbler, H.-J. (2000). Specificity in the organization of the autonomic

579 nervous system: A basis for precise neural regulation of homeostatic and protective

580 body functions. *Progress in brain research*, *122*, 351–367.

581 https://doi.org/10.1016/s0079-6123(08)62150-0

582 [30] de Gee, J. W., Knapen, T., & Donner, T. H. (2014). Decision-related pupil dilation

583 reflects upcoming choice and individual bias. *Proceedings of the National Academy*

584 *of Sciences*, *111* (5), E618–E625. https://doi.org/10.1073/pnas.1317557111

585 [31] Urai, A. E., Braun, A., & Donner, T. H. (2017). Pupil-linked arousal is driven by

586 decision uncertainty and alters serial choice bias. *Nature communications*, *8* (1),

587 1–11. https://doi.org/10.1038/ncomms14637

588 [32] Schriver, B. J., Bagdasarov, S., & Wang, Q. (2018). Pupil-linked arousal modulates

589 behavior in rats performing a whisker deflection direction discrimination task.

590 *Journal of neurophysiology*, *120* (4), 1655–1670.

591 https://doi.org/10.1152/jn.00290.2018

592 [33] Schriver, B. J., Perkins, S. M., Sajda, P., & Wang, Q. (2020). Interplay between

593 components of pupil-linked phasic arousal and its role in driving behavioral choice

594 in go/no-go perceptual decision-making. *Psychophysiology*, *57* (8), e13565.

595 https://doi.org/10.1111/psyp.13565

596 [34] Nassar, M. R., Rumsey, K. M., Wilson, R. C., Parikh, K., Heasly, B., & Gold, J. I.

597 (2012). Rational regulation of learning dynamics by pupil-linked arousal systems.

598 *Nature neuroscience*, *15* (7), 1040–1046. https://doi.org/10.1038/nn.3130

599 [35] Murphy, P. R., O'connell, R. G., O'sullivan, M., Robertson, I. H., & Balsters, J. H.

600 (2014). Pupil diameter covaries with bold activity in human locus coeruleus. *Human*

601 *brain mapping*, *35* (8), 4140–4154. https://doi.org/10.1002/hbm.22466

602 [36] Alnæs, D., Sneve, M. H., Espeseth, T., Endestad, T., van de Pavert, S. H. P., &

603 Laeng, B. (2014). Pupil size signals mental effort deployed during multiple object

604 tracking and predicts brain activity in the dorsal attention network and the locus

605 coeruleus. *Journal of vision*, *14* (4), 1–1. https://doi.org/10.1167/14.4.1

606 [37] Joshi, S., Li, Y., Kalwani, R. M., & Gold, J. I. (2016). Relationships between pupil

607 diameter and neuronal activity in the locus coeruleus, colliculi, and cingulate cortex.

608 *Neuron*, *89* (1), 221–234. https://doi.org/10.1016/j.neuron.2015.11.028

609 [38] Liu, Y., Rodenkirch, C., Moskowitz, N., Schriver, B., & Wang, Q. (2017). Dynamic

610 lateralization of pupil dilation evoked by locus coeruleus activation results from

611 sympathetic, not parasympathetic, contributions. *Cell reports*, *20* (13), 3099–3112.

612 https://doi.org/10.1016/j.celrep.2017.08.094

613 [39] Reimer, J., McGinley, M. J., Liu, Y., Rodenkirch, C., Wang, Q., McCormick, D. A.,

614 & Tolias, A. S. (2016). Pupil fluctuations track rapid changes in adrenergic and

615 cholinergic activity in cortex. *Nature communications*, *7* (1), 1–7.

616 https://doi.org/10.1038/ncomms13289

617 [40] Luppi, P.-H., Aston-Jones, G., Akaoka, H., Chouvet, G., & Jouvet, M. (1995).

618 Afferent projections to the rat locus coeruleus demonstrated by retrograde and

619 anterograde tracing with cholera-toxin b subunit and phaseolus vulgaris

620 leucoagglutinin. *Neuroscience*, *65* (1), 119–160.

621 https://doi.org/10.1016/0306-4522(94)00481-J

622 [41] Kim, M.-A., & Lee, H. S. (2003). Descending projections from the prefrontal cortex

623 to the locus coeruleus of the rat. *Korean Journal of Biological Sciences*, *7* (1), 49–55.

624 https://doi.org/10.1080/12265071.2003.9647682

625 [42] Arnsten, A., & Goldman-Rakic, P. (1984). Selective prefrontal cortical projections

626 to the region of the locus coeruleus and raphe nuclei in the rhesus monkey. *Brain*

627 *research*, *306* (1-2), 9–18. https://doi.org/10.1016/0006-8993(84)90351-2

628 [43] Sokolov, E. N. (1963). Higher nervous functions: The orienting reflex. *Annual review*

629 *of physiology*, *25* (1), 545–580. https://doi.org/10.1146/annurev.ph.25.030163.002553

630 [44] Corneil, B. D., & Munoz, D. P. (2014). Overt responses during covert orienting.

631 *Neuron*, *82* (6), 1230–1243. https://doi.org/10.1016/j.neuron.2014.05.040

632 [45] Brascamp, J. W., De Hollander, G., Wertheimer, M. D., DePew, A. N., &

633 Knapen, T. (2021). Separable pupillary signatures of perception and action during

634 perceptual multistability. *Elife*, *10*, e66161. https://doi.org/10.7554/eLife.66161

[46] Denison, R. N., Parker, J. A., & Carrasco, M. (2020). Modeling pupil responses to rapid sequential events. *Behavior research methods*, *52* (5), 1991–2007. https://doi.org/10.3758/s13428-020-01368-6

[47] Slooter, J., & Van Norren, D. (1980). Visual acuity measured with pupil responses to checkerboard stimuli. *Investigative ophthalmology & visual science*, *19* (1), 105–108.

[48] Gamlin, P. D., Zhang, H., Harlow, A., & Barbur, J. L. (1998). Pupil responses to stimulus color, structure and light flux increments in the rhesus monkey. *Vision research*, *38* (21), 3353–3358. https://doi.org/10.1016/S0042-6989(98)00096-0

[49] Barbur, J., Harlow, A., & Sahraie, A. (1992). Pupillary responses to stimulus structure, colour and movement. *Ophthalmic and Physiological Optics*, *12* (2), 137–141. https://doi.org/10.1111/j.1475-1313.1992.tb00276.x

[50] Young, R. S., Kimura, E., & Delucia, P. R. (1995). A pupillometric correlate of scotopic visual acuity. *Vision research*, *35* (15), 2235–2241. https://doi.org/10.1016/0042-6989(94)00303-3

[51] Hu, X., Hisakata, R., & Kaneko, H. (2019). Effects of spatial frequency and attention on pupillary response. *JOSA A*, *36* (10), 1699–1708. https://doi.org/10.1364/JOSAA.36.001699

[52] Naber, M., Frässle, S., & Einhäuser, W. (2011). Perceptual rivalry: Reflexes reveal the gradual nature of visual awareness. *PLoS One*, *6* (6), e20910. https://doi.org/10.1371/journal.pone.0020910

[53] Kanari, K., & Kaneko, H. (2021). Pupil response is modulated with optokinetic nystagmus in transparent motion. *JOSA A*, *38* (2), 149–156. https://doi.org/10.1364/JOSAA.409940

[54] Nakano, T., Ichiki, A., & Fujikado, T. (2021). Pupil constriction via the parasympathetic pathway precedes perceptual switch of ambiguous stimuli. *International Journal of Psychophysiology*, *167*, 15–21. https://doi.org/10.1016/j.ijpsycho.2021.06.006

[55] van Hooijdonk, R., Mathôt, S., Schat, E., Spencer, H., van der Stigchel, S., & Dijkerman, H. C. (2019). Touch-induced pupil size reflects stimulus intensity, not

664   subjective pleasantness. *Experimental brain research*, *237* (1), 201–210.

665   https://doi.org/10.1007/s00221-018-5404-2

666   [56] Wetzel, N., Buttelmann, D., Schieler, A., & Widmann, A. (2016). Infant and adult

667   pupil dilation in response to unexpected sounds. *Developmental psychobiology*,

668   *58* (3), 382–392. https://doi.org/10.1002/dev.21377

669   [57] Knapen, T., de Gee, J. W., Brascamp, J., Nuiten, S., Hoppenbrouwers, S., &

670   Theeuwes, J. (2016). Cognitive and ocular factors jointly determine pupil responses

671   under equiluminance. *PloS one*, *11* (5), e0155574.

672   https://doi.org/10.1371/journal.pone.0155574

673   [58] Bertheaux, C., Toscano, R., Fortunier, R., Roux, J.-C., Charier, D., & Borg, C.

674   (2020). Emotion measurements through the touch of materials surfaces. *Frontiers in*

675   *human neuroscience*, *13*, 455. https://doi.org/10.3389/fnhum.2019.00455

676   [59] Wang, C.-A., Boehnke, S. E., Itti, L., & Munoz, D. P. (2014). Transient pupil

677   response is modulated by contrast-based saliency. *Journal of Neuroscience*, *34* (2),

678   408–417. https://doi.org/10.1523/JNEUROSCI.3550-13.2014

679   [60] Mathôt, S., & Van der Stigchel, S. (2015). New light on the mind's eye: The

680   pupillary light response as active vision. *Current directions in psychological science*,

681   *24* (5), 374–378. https://doi.org/10.1177/0963721415593725

682   [61] Binda, P., & Gamlin, P. D. (2017). Renewed attention on the pupil light reflex.

683   *Trends in Neurosciences*, *40* (8), 455–457. https://doi.org/10.1016/j.tins.2017.06.007

684   [62] Strauch, C., Romein, C., Naber, M., Van der Stigchel, S., & Ten Brink, A. F.

685   (2022). The orienting response drives pseudoneglect - evidence from an objective

686   pupillometric method. *Cortex*. https://doi.org/10.1016/j.cortex.2022.03.006

687   [63] Stein, B. E., & Meredith, M. A. (1993). *The merging of the senses.* The MIT press.

688   [64] Leichnetz, G., Spencer, R., Hardy, S., & Astruc, J. (1981). The prefrontal

689   corticotectal projection in the monkey; an anterograde and retrograde horseradish

690   peroxidase study. *Neuroscience*, 6 (6), 1023–1041. https://doi.org/10.1016/0306-

691   4522(81)90068-3

692   [65] Sara, S. J., & Bouret, S. (2012). Orienting and reorienting: The locus coeruleus

693   mediates cognition through arousal. *Neuron*, *76* (1), 130–141.

694   https://doi.org/10.1016/j.neuron.2012.09.011

695   [66] Bell, A. H., Fecteau, J. H., & Munoz, D. P. (2004). Using auditory and visual

696   stimuli to investigate the behavioral and neuronal consequences of reflexive covert

697   orienting. *Journal of neurophysiology*, *91* (5), 2172–2184.

698   https://doi.org/10.1152/jn.01080.2003

699   [67] Aston-Jones, G., Rajkowski, J., Kubiak, P., & Alexinsky, T. (1994). Locus coeruleus

700   neurons in monkey are selectively activated by attended cues in a vigilance task.

701   *Journal of Neuroscience*, *14* (7), 4467–4480.

702   https://doi.org/10.1523/JNEUROSCI.14-07-04467.1994

703   [68] Binda, P., & Murray, S. O. (2015). Keeping a large-pupilled eye on high-level visual

704   processing. *Trends in cognitive sciences*, *19* (1), 1–3.

705   https://doi.org/10.1016/j.tics.2014.11.002

706   [69] Fahle, M. W., Stemmler, T., & Spang, K. M. (2011). How much of the

707   "unconscious" is just pre–threshold? *Frontiers in Human Neuroscience*, *5*, 120.

708   https://doi.org/10.3389/fnhum.2011.00120

709   [70] Laeng, B., & Sulutvedt, U. (2014). The eye pupil adjusts to imaginary light.

710   *Psychological Science*, *25* (1), 188–197. https://doi.org/10.1177/0956797613503556

711   [71] Laeng, B., & Endestad, T. (2012). Bright illusions reduce the eye's pupil.

712   *Proceedings of the National Academy of Sciences*, *109* (6), 2162–2167.

713   [72] Binda, P., Pereverzeva, M., & Murray, S. O. (2013). Attention to bright surfaces

714   enhances the pupillary light reflex. *Journal of Neuroscience*, *33* (5), 2199–2204.

715   https://doi.org/10.1523/JNEUROSCI.3440-12.2013

716   [73] Naber, M., & Nakayama, K. (2013). Pupil responses to high-level image content.

717   *Journal of vision*, *13* (6), 7–7. https://doi.org/10.1167/13.6.7

718   [74] Sapir, A., Hershman, R., & Henik, A. (2021). Top-down effect on pupillary

719   response: Evidence from shape from shading. *Cognition*, *212*, 104664.

720   https://doi.org/10.1016/j.cognition.2021.104664

721   [75] Sulutvedt, U., Mannix, T. K., & Laeng, B. (2018). Gaze and the eye pupil adjust to

722   imagined size and distance. *Cognitive science*, *42* (8), 3159–3176.

723   https://doi.org/10.1111/cogs.12684

724   [76] Naber, M., Alvarez, G. A., & Nakayama, K. (2013). Tracking the allocation of

725   attention using human pupillary oscillations. *Frontiers in psychology*, *4*, 919.

726   https://doi.org/10.3389/fpsyg.2013.00919

727   [77] Salvaggio, S., Andres, M., Zénon, A., & Masson, N. (2022). Pupil size variations

728   reveal covert shifts of attention induced by numbers. *Psychonomic Bulletin &*

729   *Review*, 1–10. https://doi.org/10.3758/s13423-022-02094-0

730   [78] Mathôt, S., Melmi, J.-B., Van Der Linden, L., & Van der Stigchel, S. (2016). The

731   mind-writing pupil: A human-computer interface based on decoding of covert

732   attention through pupillometry. *PloS one*, *11* (2), e0148805.

733   https://doi.org/10.1371/journal.pone.0148805

734   [79] Tononi, G., Srinivasan, R., Russell, D. P., & Edelman, G. M. (1998). Investigating

735   neural correlates of conscious perception by frequency-tagged neuromagnetic

736   responses. *Proceedings of the National Academy of Sciences*, *95* (6), 3198–3203.

737   [80] Bradley, M. M., Miccoli, L., Escrig, M. A., & Lang, P. J. (2008). The pupil as a

738   measure of emotional arousal and autonomic activation. *Psychophysiology*, *45* (4),

739   602–607.

740   https://doi.org/10.1111/j.1469-8986.2008.00654.x;10.1111/j.1469-8986.2008.00654.x

741   [81] Kang, O., & Wheatley, T. (2017). Pupil dilation patterns spontaneously synchronize

742   across individuals during shared attention. *Journal of Experimental Psychology:*

743   *General*, *146* (4), 569. https://doi.org/10.1037/xge0000271

744   [82] van Olst, E. H., Heemstra, M. L., & ten Kortenaar, T. (2021). 30 stimulus

745   significance and the orienting reaction. *The Orienting Reflex in Humans: An*

746   *International Conference Sponsored by the Scientific Affairs Division of the North*

747   *Atlantic Treaty Organization*, 12.

748   [83] Wierda, S. M., van Rijn, H., Taatgen, N. A., & Martens, S. (2012). Pupil dilation

749   deconvolution reveals the dynamics of attention at high temporal resolution.

750   *Proceedings of the National Academy of Sciences*, *109* (22), 8456–8460.

751   https://doi.org/10.1073/pnas.1201858109

752 [84] Kloosterman, N. A., Meindertsma, T., van Loon, A. M., Lamme, V. A.,

753   Bonneh, Y. S., & Donner, T. H. (2015). Pupil size tracks perceptual content and

754   surprise. *European Journal of Neuroscience*, *41* (8), 1068–1078.

755   https://doi.org/10.1111/ejn.12859

756 [85] Hupé, J.-M., Lamirel, C., & Lorenceau, J. (2009). Pupil dynamics during bistable

757   motion perception. *Journal of vision*, *9* (7), 10–10. https://doi.org/10.1167/9.7.10

758 [86] Einhäuser, W., Stout, J., Koch, C., & Carter, O. (2008). Pupil dilation reflects

759   perceptual selection and predicts subsequent stability in perceptual rivalry.

760   *Proceedings of the National Academy of Sciences*, *105* (5), 1704–1709.

761   https://doi.org/10.1073/pnas.0707727105

762 [87] Castaldi, E., Pomè, A., Cicchini, G. M., Burr, D., & Binda, P. (2021). The pupil

763   responds spontaneously to perceived numerosity. *Nature communications*, *12* (1), 1–

764   8. https://doi.org/10.1038/s41467-021-26261-4

765 [88] Barbur, J. L., & Thomson, W. D. (1987). Pupil response as an objective measure of

766   visual acuity. *Ophthalmic and Physiological Optics*, *7* (4), 425–429.

767 [89] Conway, C. A., Jones, B. C., DeBruine, L., Little, A., & Sahraie, A. (2008).

768   Transient pupil constrictions to faces are sensitive to orientation and species.

769   *Journal of Vision*, *8* (3), 17–17. https://doi.org/10.1167/8.3.17

770 [90] Sterpenich, V., D'Argembeau, A., Desseilles, M., Balteau, E., Albouy, G.,

771   Vandewalle, G., Degueldre, C., Luxen, A., Collette, F., & Maquet, P. (2006). The

772   locus ceruleus is involved in the successful retrieval of emotional memories in

773   humans. *Journal of Neuroscience*, *26* (28), 7416–7423.

774   https://doi.org/10.1523/JNEUROSCI.1001-06.2006.

775 [91] Naber, M., Frässle, S., Rutishauser, U., & Einhäuser, W. (2013). Pupil size signals

776   novelty and predicts later retrieval success for declarative memories of natural

777   scenes. *Journal of vision*, *13* (2), 11–11. https://doi.org/10.1167/13.2.11

778 [92] Naber, M., Hilger, M., & Einhäuser, W. (2012). Animal detection and identification

779   in natural scenes: Image statistics and emotional valence. *Journal of vision*, *12* (1),

780   25–25. https://doi.org/10.1167/12.1.25

781   [93]   Wang, C.-A., & Munoz, D. P. (2018). Neural basis of location-specific pupil

782   luminance modulation. *Proceedings of the National Academy of Sciences*, 201809668.

783   https://doi.org/10.1073/pnas.1809668115

784   [94]   Stanton, G. B., Bruce, C. J., & Goldberg, M. E. (1995). Topography of projections

785   to posterior cortical areas from the macaque frontal eye fields. *Journal of*

786   *Comparative Neurology, 353* (2). https://doi.org/10.1002/cne.903530210

787   [95]   Kunzle, H., & Akert, K. (1977). Efferent connections of cortical, area 8 (frontal eye

788   field) in Macaca fascicularis. A reinvestigation using the autoradiographic technique.

789   *Journal of Comparative Neurology, 173* (1). https://doi.org/10.1002/cne.901730108

790   [96]   Ebitz, R. B., & Platt, M. L. (2015). Neuronal activity in primate dorsal anterior

791   cingulate cortex signals task conflict and predicts adjustments in pupil-linked

792   arousal. *Neuron, 85* (3), 628–640.

793   https://doi.org/10.1016/j.neuron.2014.12.053;10.1016/j.neuron.2014.12.053

794   [97]   Joshi, S., & Gold, J. I. (2019). Context-Dependent Relationships between Locus

795   Coeruleus Activation and Coordinated Neural Activity Patterns in the Anterior

796   Cingulate Cortex. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.3413098

797   [98]   Varazzani, C., San-Galli, A., Gilardeau, S., & Bouret, S. (2015). Noradrenaline and

798   dopamine neurons in the reward/effort trade-off: A direct electrophysiological

799   comparison in behaving monkeys. *Journal of Neuroscience, 35* (20), 7866–7877.

800   https://doi.org/10.1523/JNEUROSCI.0454-15.2015

801   [99]   Breton-Provencher, V., & Sur, M. (2019). Active control of arousal by a locus

802   coeruleus gabaergic circuit. *Nature neuroscience, 22* (2), 218–228.

803   https://doi.org/10.1038/s41593-018-0305-z

804   [100] Megemont, M., McBurney-Lin, J., & Yang, H. (2022). Pupil diameter is not an

805   accurate real-time readout of locus coeruleus activity. *Elife, 11*, e70510.

806   https://doi.org/10.7554/eLife.70510.sa0

807   [101] Krauzlis, R. J., Lovejoy, L. P., & Zénon, A. (2013). Superior colliculus and visual

808   spatial attention. *Annual review of neuroscience, 36*, 165–182.

809   https://doi.org/10.1146/annurev-neuro-062012-170249

810   [102] Wang, C.-A., & Munoz, D. P. (2021). Coordination of pupil and saccade responses

811   by the superior colliculus. *Journal of Cognitive Neuroscience*, *33* (5), 919–932.

812   https://doi.org/10.1162/jocn_a_01688

813   [103] Wang, C.-A., Boehnke, S. E., White, B. J., & Munoz, D. P. (2012).

814   Microstimulation of the monkey superior colliculus induces pupil dilation without

815   evoking saccades. *Journal of Neuroscience*, *32* (11), 3629–3636.

816   https://doi.org/10.1523/JNEUROSCI.5512-11.2012

817   [104] Lehmann, S. J., & Corneil, B. D. (2016). Transient pupil dilation after subsaccadic

818   microstimulation of primate frontal eye fields. *Journal of Neuroscience*, *36* (13),

819   3765–3776. https://doi.org/10.1523/JNEUROSCI.4264-15.2016

820   [105] Ebitz, R. B., & Moore, T. (2017). Selective modulation of the pupil light reflex by

821   microstimulation of prefrontal cortex. *Journal of Neuroscience*, *37* (19), 5008–5018.

822   https://doi.org/10.1523/JNEUROSCI.2433-16.2017

823   [106] May, P. J., Warren, S., Bohlen, M. O., Barnerssoi, M., & Horn, A. K. E. (2016). A

824   central mesencephalic reticular formation projection to the Edinger-Westphal nuclei.

825   *Brain structure function*, *221* (8), 4073–4089.

826   https://doi.org/10.1007/s00429-015-1147-z

827   [107] May, P. J. (2006). The mammalian superior colliculus: laminar structure and

828   connections. *Progress in brain research*, *151*, 321–378.

829   https://doi.org/10.1016/S0079-6123(05)51011-2

830   [108] Barnerssoi, M., May, P. J., & Horn, A. K. E. (2017). GABAergic innervation of the

831   ciliary ganglion in macaque monkeys - A light and electron microscopic study.

832   *Journal of Comparative Neurology*, *525* (7), 1517–1531.

833   https://doi.org/10.1002/cne.24145

834   [109] Perkins, E., Warren, S., & May, P. J. (2009). The mesencephalic reticular formation

835   as a conduit for primate collicular gaze control: Tectal inputs to neurons targeting

836   the spinal cord and medulla. *The Anatomical Record: Advances in Integrative*

837   *Anatomy and Evolutionary Biology: Advances in Integrative Anatomy and*

838   *Evolutionary Biology*, *292* (8), 1162–1181. https://doi.org/10.1002/ar.20935

839   [110]   Nelson, A., & Mooney, R. (2016). The basal forebrain and motor cortex provide

840   convergent yet distinct movement-related inputs to the auditory cortex. *Neuron*, *90*

841   (3), 635–648. https://doi.org/10.1016/j.neuron.2016.03.031

842   [111]   Dringenberg, H., & Olmstead, M. (2003). Integrated contributions of basal forebrain

843   and thalamus to neocortical activation elicited by pedunculopontine tegmental

844   stimulation in urethane-anesthetized rats. *Neuroscience*, *119* (3), 839–853.

845   https://doi.org/10.1016/S0306-4522(03)00197-0

846   [112]   Aizawa, H., Kobayashi, Y., Yamamoto, M., & Isa, T. (1999). Injection of nicotine

847   into the superior colliculus facilitates occurrence of express saccades in monkeys.

848   *Journal of neurophysiology*, *82* (3), 1642–1646.

849   https://doi.org/10.1152/jn.1999.82.3.1642

850   [113]   Boucsein, W. (2012). *Electrodermal activity*. Springer Science+Business Media,

851   LLC. https://doi.org/10.1007/978-1-4614-1126-0

852   [114]   Mendelowitz, D. (1999). Advances in Parasympathetic Control of Heart Rate and

853   Cardiac Function. *News in physiological sciences : an international journal of*

854   *physiology produced jointly by the International Union of Physiological Sciences and*

855   *the American Physiological Society*, *14*, 155–161.

856   http://www.ncbi.nlm.nih.gov/pubmed/11390842

857   [115]   Friedman, D., Hakerem, G., Sutton, S., & Fleiss, J. L. (1973). Effect of stimulus

858   uncertainty on the pupillary dilation response and the vertex evoked potential.

859   *Electroencephalography and clinical neurophysiology*, *34* (5), 475–484.

860   [116]   Gomez, P., von Gunten, A., & Danuser, B. (2016). Autonomic nervous system

861   reactivity within the valence-arousal affective space: Modulation by sex and age.

862   *International journal of psychophysiology*, *109*, 51–62.

863   https://doi.org/10.1016/j.ijpsycho.2016.10.002

864   [117]   Wang, C.-A., Baird, T., Huang, J., Coutinho, J. D., Brien, D. C., & Munoz, D. P.

865   (2018). Arousal Effects on Pupil Size, Heart Rate, and Skin Conductance in an

866   Emotional Face Task. *Frontiers in Neurology*, *9* (December), 1–13.

867   https://doi.org/10.3389/fneur.2018.01029

868   [118]   Jennings, J. R., van der Molen, M. W., & Steinhauer, S. R. (1998). Preparing the

869   heart, eye, and brain: foreperiod length effects in a nonaging paradigm.

870   *Psychophysiology*, *35* (1), 90–98. http://www.ncbi.nlm.nih.gov/pubmed/9499710

871   [119]   Gergelyfi, M., Jacob, B., Olivier, E., & Zénon, A. (2015). Dissociation between

872   mental fatigue and motivational state during prolonged mental activity. *Frontiers in*

873   *Behavioral Neuroscience*, *9* (July). https://doi.org/10.3389/fnbeh.2015.00176

874   [120]   Schumann, A., Kietzer, S., Ebel, J., & Bär, K. J. (2020). Sympathetic and

875   Parasympathetic Modulation of Pupillary Unrest. *Frontiers in Neuroscience*, *14*,

876   178. https://doi.org/10.3389/fnins.2020.00178

877   [121]   Leuchs, L., Schneider, M., & Spoormaker, V. I. (2019). Measuring the conditioned

878   response: A comparison of pupillometry, skin conductance, and startle

879   electromyography. *Psychophysiology*, *56* (1). https://doi.org/10.1111/psyp.13283

880   [122]   Jentsch, V. L., Wolf, O. T., & Merz, C. J. (2020). Temporal dynamics of

881   conditioned skin conductance and pupillary responses during fear acquisition and

882   extinction. *International Journal of Psychophysiology*, *147*.

883   https://doi.org/10.1016/j.ijpsycho.2019.11.006

884   [123]   Liu, Y., Narasimhan, S., Schriver, B. J., & Wang, Q. (2021). Perceptual Behavior

885   Depends Differently on Pupil-Linked Arousal and Heartbeat Dynamics-Linked

886   Arousal in Rats Performing Tactile Discrimination Tasks. *Frontiers in Systems*

887   *Neuroscience*, *14*. https://doi.org/10.3389/fnsys.2020.614248

888   [124]   Nieuwenhuis, S., De Geus, E. J., & Aston-Jones, G. (2011). The anatomical and

889   functional relationship between the p3 and autonomic components of the orienting

890   response. *Psychophysiology*, *48* (2), 162–175. https://doi.org/10.1111/j.1469-

891   8986.2010.01057.x

892   [125]   Derksen, M., van Alphen, J., Schaap, S., Mathot, S., & Naber, M. (2018). Pupil

893   mimicry is the result of brightness perception of the iris and pupil. *Journal of*

894   *cognition*, *1* (1). https://doi.org/10.5334/joc.34

895   [126]   Laeng, B., Kiambarua, K. G., Hagen, T., Bochynska, A., Lubell, J., Suzuki, H., &

896   Okubo, M. (2018). The" face race lightness illusion": An effect of the eyes and

897   pupils? *Plos one*, *13* (8), e0201603. https://doi.org/10.1371/journal.pone.0201603

898   [127]   Kardon, R. H., Kirkali, P. A., & Thompson, H. S. (1991). Automated pupil

899   perimetry pupil field mapping in patients and normal subjects. *Ophthalmology*,

900   *98* (4), 485–496.

901   [128]   Yoo, K., Ahn, J., & Lee, S.-H. (2021). The confounding effects of eye blinking on

902   pupillometry, and their remedy. *PloS one*, *16* (12), e0261463.

903   https://doi.org/10.1371/journal.pone.0261463

904   [129]   Cherng, Y.-G., Baird, T., Chen, J.-T., & Wang, C.-A. (2020). Background

905   luminance effects on pupil size associated with emotion and saccade preparation.

906   *Scientific reports*, *10* (1), 1–11. https://doi.org/10.1038/s41598-020-72954-z

907   [130]   Hayes, T. R., & Petrov, A. A. (2016). Mapping and correcting the influence of gaze

908   position on pupil size measurements. *Behavior Research Methods*, *48* (2), 510–527.

909   https://doi.org/10.3758/s13428-015-0588-x

910   [131]   Hoeks, B., & Levelt, W. J. (1993). Pupillary dilation as a measure of attention: A

911   quantitative system analysis. *Behavior Research Methods, Instruments, &*

912   *Computers*, *25* (1), 16–26. https://doi.org/10.3758/BF03204445

913   [132]   Mathôt, S., Fabius, J., Van Heusden, E., & Van der Stigchel, S. (2018). Safe and

914   sensible preprocessing and baseline correction of pupil-size data. *Behavior research*

915   *methods*, *50* (1), 94–106. https://doi.org/10.3758/s13428-017-1007-2

916   [133]   Reilly, J., Kelly, A., Kim, S. H., Jett, S., & Zuckerman, B. (2019). The human

917   task-evoked pupillary response function is linear: Implications for baseline response

918   scaling in pupillometry. *Behavior research methods*, *51* (2), 865–878.

919   https://doi.org/10.3758/s13428-018-1134-4

920   [134]   Kelbsch, C., Strasser, T., Chen, Y., Feigl, B., Gamlin, P. D., Kardon, R., Peters, T.,

921   Roecklein, K. A., Steinhauer, S. R., Szabadi, E. et al. (2019). Standards in

922   pupillography. *Frontiers in Neurology*, 129.

923   https://doi.org/10.3389/fneur.2019.00129

924   [135]   Jackson, I., & Sirois, S. (2009). Infant cognition: Going full factorial with pupil

925   dilation. *Developmental science*, *12* (4), 670–679.

926   https://doi.org/10.1111/j.1467-7687.2008.00805.x

927   [136]   Friston, K. J., Holmes, A., Poline, J.-B., Price, C. J., & Frith, C. D. (1996).

928   Detecting activations in pet and fmri: Levels of inference and power. *Neuroimage*,

929   *4* (3), 223–235. https://doi.org/10.1006/nimg.1996.0074

930   [137]   Turi, M., Burr, D. C., & Binda, P. (2018). Pupillometry reveals perceptual

931   differences that are tightly linked to autistic traits in typical adults. *Elife*, *7*, e32399.

932   https://doi.org/10.7554/eLife.32399.001

933   [138]   Laeng, B., Færevaag, F. S., Tanggaard, S., & von Tetzchner, S. (2018). Pupillary

934   responses to illusions of brightness in autism spectrum disorder. *i-Perception*, *9* (3),

935   2041669518771716. https://doi.org/10.1177/2041669518771716

936   [139]   Kardon, R. H. (1992). Pupil perimetry. *Current Opinion in Ophthalmology*, *3* (5),

937   565–570. https://doi.org/10.1097/00055735-199210000-00002

938   [140]   Schmid, R., Luedtke, H., Wilhelm, B., & Wilhelm, H. (2005). Pupil campimetry in

939   patients with visual field loss. *European journal of neurology*, *12* (8), 602–608.

940   https://doi.org/10.1111/j.1468-1331.2005.01048.x

941   [141]   Carle, C. F., James, A. C., Kolic, M., Loh, Y.-W., & Maddess, T. (2011).

942   High-resolution multifocal pupillographic objective perimetry in glaucoma.

943   *Investigative ophthalmology & visual science*, *52* (1), 604–610.

944   https://doi.org/10.1167/iovs.10-5737

945   [142]   Naber, M., Roelofzen, C., Fracasso, A., Bergsma, D. P., van Genderen, M.,

946   Porro, G. L., & Dumoulin, S. O. (2018). Gaze-contingent flicker pupil perimetry

947   detects scotomas in patients with cerebral visual impairments or glaucoma.

948   *Frontiers in neurology*, *9*, 558. https://doi.org/10.3389/fneur.2018.00558

949   [143]   Ponzio, F., Villalobos, A. E. L., Mesin, L., de'Sperati, C., & Roatta, S. (2019). A

950   human-computer interface based on the "voluntary" pupil accommodative response.

951   *International Journal of Human-Computer Studies*, *126*, 53–63.

952   https://doi.org/10.1016/j.ijhcs.2019.02.002

953   [144]   Stoll, J., Chatelle, C., Carter, O., Koch, C., Laureys, S., & Einhäuser, W. (2013).

954 Pupil responses allow communication in locked-in syndrome patients. *Current*

955 *biology*, *23* (15), R647–R648. https://doi.org/10.1016/j.cub.2013.06.011

956 [145] Strauch, C., Hirzle, T., Van der Stigchel, S., & Bulling, A. (2021). Decoding binary

957 decisions under differential target probabilities from pupil dilation: A random forest

958 approach. *Journal of Vision*, *21* (7), 6–6. https://doi.org/10.1167/jov.21.7.6

959 [146] Ehlers, J., Strauch, C., Georgi, J., & Huckauf, A. (2016). Pupil size changes as an

960 active information channel for biofeedback applications. *Applied Psychophysiology*

961 *and Biofeedback*, *41* (3), 331–339. https://doi.org/10.1007/s10484-016-9335-z

962 [147] de Rooij, A., Schraffenberger, H., & Bontje, M. (2018). Augmented metacognition:

963 Exploring pupil dilation sonification to elicit metacognitive awareness. *Proceedings*

964 *of the Twelfth International Conference on Tangible, Embedded, and Embodied*

965 *Interaction*, 237–244. https://doi.org/10.1145/3173225.3173265

966 [148] Strauch, C., Barthelmaes, M., Altgassen, E., & Huckauf, A. (2020). Pupil dilation

967 fulfills the requirements for dynamic difficulty adjustment in gaming on the example

968 of pong. *ACM Symposium on Eye Tracking Research and Applications*, 1–9.

969 https://doi.org/10.1145/3379157.3388934

970 [149] Palinko, O., Kun, A. L., Shyrokov, A., & Heeman, P. (2010). Estimating cognitive

971 load using remote eye tracking in a driving simulator. *Proceedings of the 2010*

972 *symposium on eye-tracking research & applications*, 141–144.

973 https://doi.org/10.1145/1743666.1743701

974 [150] Koelewijn, T., Zekveld, A. A., Festen, J. M., Rönnberg, J., & Kramer, S. E. (2012).

975 Processing load induced by informational masking is related to linguistic abilities.

976 *International journal of otolaryngology*, *2012*. https://doi.org/10.1155/2012/865731

977 [151] Kuchinsky, S. E., Ahlstrom, J. B., Vaden Jr, K. I., Cute, S. L., Humes, L. E.,

978 Dubno, J. R., & Eckert, M. A. (2013). Pupil size varies with word listening and

979 response selection difficulty in older adults with hearing loss. *Psychophysiology*,

980 *50* (1), 23–34. https://doi.org/10.1111/j.1469-8986.2012.01477.x

981 [152] Winn, M. B., Edwards, J. R., & Litovsky, R. Y. (2015). The impact of auditory

982 spectral resolution on listening effort revealed by pupil dilation. *Ear and hearing*,

983   *36* (4), e153. https://doi.org/10.1097/AUD.000000000000145