1   **TITLE:** Trained-feature specific offline learning in an orientation detection task

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3   **RUNNING TITLE:** Sleep enhances trained-feature specific learning

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19 **ABSTRACT:**

20 It has been suggested that sleep provides additional enhancement of visual perceptual learning

21 (VPL) acquired before sleep, termed offline performance gains. A majority of the studies that

22 found offline performance gains of VPL used discrimination tasks including the texture

23 discrimination task (TDT). This makes it questionable whether offline performance gains on

24 VPL are generalized to other visual tasks. The present study examined whether a Gabor

25 orientation detection task, which is a standard task in VPL, shows offline performance gains. In

26 Experiment 1, we investigated whether sleep leads to offline performance gains on the task.

27 Subjects were trained with the Gabor orientation detection task, and re-tested it after a 12-hr

28 interval that included either nightly sleep or only wakefulness. We found that performance on the

29 task improved to a significantly greater degree after the interval that included sleep and

30 wakefulness than the interval including wakefulness alone. In addition, offline performance

31 gains were specific to the trained orientation. In Experiment 2, we tested whether offline

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32   performance gains occur by a nap. Also, we tested whether spontaneous sigma activity in early

33   visual areas during non-rapid eye movement (NREM) sleep, previously implicated in offline

34   performance gains of TDT, was associated with offline performance gains of the task. A

35   different group of subjects had a nap with polysomnography. The subjects were trained with the

36   task before the nap and re-tested after the nap. The performance of the task improved

37   significantly after the nap only on the trained orientation. Sigma activity in the trained region of

38   early visual areas during NREM sleep was significantly larger than in the untrained region, in

39   correlation with offline performance gains. These aspects were also found with VPL of TDT.

40   The results of the present study demonstrate that offline performance gains are not specific to a

41   discrimination task such as TDT, and can be generalized to other forms of VPL tasks, along with

42   trained-feature specificity. Moreover, the present results also suggest that sigma activity in the

43   trained region of early visual areas plays an important role in offline performance gains of VPL

44   of detection as well as discrimination tasks.

45

Introduction

After the initial acquisition of a skill, a learning state goes through an offline process, through which further improvement on performance is achieved without actual training (Karni et al., 1998; Walker, 2005), termed offline performance gains. It has been suggested that sleep plays an essential role in offline performance gains in various types of learning (Gais et al., 2000; Maquet et al., 2000; Stickgold et al., 2000a; Stickgold et al., 2000b; Laureys et al., 2001; Gais et al., 2002; Walker et al., 2002; Mednick et al., 2003; Huber et al., 2004; Stickgold, 2005; Walker, 2005; Walker and Stickgold, 2005; Walker et al., 2005; Matarazzo et al., 2008; Tamaki et al., 2008; Yotsumoto et al., 2009b; Diekelmann and Born, 2010; Born and Wilhelm, 2012; Mascetti et al., 2013; Rasch and Born, 2013; Tamaki et al., 2013; Bang et al., 2014; McDevitt et al., 2014; Tononi and Cirelli, 2014). One type of learning for which sleep is beneficial is visual perceptual learning (VPL) (Karni et al., 1994; Gais et al., 2000; Stickgold et al., 2000a; Mednick et al., 2003; Censor et al., 2006; Yotsumoto et al., 2009b; Bang et al., 2014). VPL refers to a long-lasting performance improvement on a visual task after visual experience (Sasaki et al., 2010; Lu et al., 2011; Sagi, 2011), and has been proposed to primarily involve reorganization in early visual areas (Schoups et al., 2001; Schwartz et al., 2002; Shibata et al., 2017) (but see other studies (Law and Gold, 2008; Xiao et al., 2008)). After sleep, either night sleep or a daytime nap, the performance on VPL is significantly enhanced compared to that before sleep. In addition, the amount of improvement after sleep surpasses that after the same amount of time, which does not include sleep (Karni et al., 1994; Gais et al., 2000; Stickgold et al., 2000a; Mednick et al., 2003; Censor et al., 2006; Yotsumoto et al., 2009b; Bang et al., 2014).

However, it remains to be elucidated whether offline performance gains are generalized to VPL tasks. The majority of studies which found that sleep plays a role in the performance gain in VPL used the texture discrimination task (or 'TDT'), which is a standard task in VPL (Karni et al., 1994; Gais et al., 2000; Stickgold et al., 2000a; Mednick et al., 2003; Censor et al., 2006; Yotsumoto et al., 2009b; Bang et al., 2014). Curiously, other studies that found offline performance gains of sleep in VPL also used a discrimination task, including coarse orientation discrimination (Matarazzo et al., 2008; Mascetti et al., 2013) and motion direction discrimination tasks (McDevitt et al., 2014). Importantly, it has been suggested that the underlying mechanisms between a detection task and a discrimination task are significantly different (Regan and

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77   Beverley, 1985; Jazayeri and Movshon, 2006; Bridwell et al., 2013). This raises the question as

78   to whether sleep is effective on VPL in general, including a detection task, or whether the effect

79   of sleep on VPL is specific to discrimination tasks.

80   In addition, it is controversial which spontaneous brain activity during sleep is involved

81   in offline performance gains of VPL. Sleep spindles (13-16 Hz) are characteristic spontaneous

82   brain activity during non-rapid eye movement (NREM) sleep typically used for sleep stage

83   scoring and appear around the central brain regions. Sleep spindles have been shown to be

84   involved in motor memory in human (Manoach and Stickgold, 2009; Manoach et al., 2010;

85   Tamaki et al., 2013; Manoach et al., 2016; Laventure et al., 2018) and have been suggested to

86   enhance plasticity (Sejnowski and Destexhe, 2000; Rosanova and Ulrich, 2005). Sigma activity

87   (13-16 Hz) is a spontaneous oscillatory activity during sleep whose frequency corresponds to

88   sleep spindles. Since VPL is assumed to involve early visual areas, instead of typical sleep

89   spindles appearing around the central brain regions, previously we measured the strength of

90   regional sigma activity from early visual areas during sleep and found the correlation with the

91   degree of offline performance gains of TDT (Bang et al., 2014). In the current study, we tested

92   whether regional sigma activity in early visual areas is also involved in offline performance gains

93   of the Gabor orientation detection task.

94   First, the results show that the performance on the Gabor orientation detection task

95   improved significantly after the night of sleep without any additional training. No such offline

96   performance gain was found after the same amount of interval that included only wakefulness.

97   Second, we found that offline performance gains occur after a daytime nap as well. Moreover,

98   sigma activity was significantly larger in the trained region than in the untrained region in early

99   visual areas. The performance improvement over the nap significantly correlated with the power

100   of sigma activity in the trained region of early visual areas. The present results suggest that

101   offline performance gains occur not only a discrimination task but also in a detection task, and

102   that sigma activity in the trained region of early visual areas during sleep may play a common

103   role in offline performance gains of VPL.

104

105   **Material and Methods**

106   *Participants*

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107   We conducted a careful screening process for eligibility for participation, since various

108   factors are known to influence visual sensitivity and sleep structures. All the subjects had no

109   prior experience in VPL tasks, as experiences in VPL tasks may cause a long-term visual

110   sensitivity change (Karni and Sagi, 1991; Schwartz et al., 2002; Seitz et al., 2005; Yotsumoto et

111   al., 2009a; Sasaki et al., 2010; Lu et al., 2011; Sagi, 2011). People who play action video games

112   frequently were excluded because extensive video game playing affects visual and attention

113   processing (Green and Bavelier, 2003; Li et al., 2009; Berard et al., 2015). In addition, subjects

114   were required to have a regular sleep schedule and anyone who had a physical or psychiatric

115   disease, was currently under medication, or was suspected to have a sleep disorder was excluded,

116   as these factors are known to impact sleep structures (Horikawa et al., 2013; Tamaki et al., 2014;

117   2016). None had medical conditions, including sleep disorders according to the self-reports. All

118   subjects gave written informed consent for their participation in experiments. This study was

119   approved at the institutional review board at Brown University.

120   A total of seventeen young healthy subjects with normal or corrected-to-normal vision

121   participated in the study. A total of eight subjects participated in Experiment 1. They were

122   randomly assigned to the sleep group (four subjects; 3 females, 20.0 ± 0.48 years old, mean $\pm$

123   SEM) or to the wake group (four subjects; 3 females, 23.0 ± 1.22 years old, mean $\pm$ SEM). A

124   total of nine subjects (4 females, 24.3 ± 0.55 years old, mean $\pm$ SEM) participated in Experiment

125   2. In Experiment 2, which was a within-subject design, all subjects had a nap.

126

127   ***Experimental design for Experiment 1***

128   The subjects in the sleep group arrived at the experimental room at 9 pm. We explained how to

129   perform the task (the introductory session, see below). Then the subjects performed a pre-

130   training test session of the orientation detection task (see ***Orientation detection task*** below) to

131   measure their initial performance level before training (**Fig. 1A, Sleep group**). After the pre-

132   training test session, which took approximately 5 min, the subjects underwent intensive training

133   on the task for approximately 45 min. After the training session, a post-training test session

134   (approximately 5 min) was conducted to measure the performance change by training. These 3

135   sessions (pre-training test, training, post-training test) lasted about one hour in total to complete.

136   There were approximately 2-min breaks between the pre-training test and the onset of training

137   sessions, as well as between the training and the onset of post-training test sessions. After the

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138 completion of the post-training test session, the subjects slept at their home. In the next morning

139 (9am), the subjects performed a post-interval test session. The post-interval test session lasted

140 approximately 5 min.

141 The subjects in the control wake group arrived at the experimental room at 9 am. After

142 the introduction session, they performed a pre-training test session, training session and a post-

143 training test session, with 2-min break in-between. These sessions took place in the morning

144 between 9-10am (**Fig. 1A, Wake group**). At 9 pm on the same day, they performed a post-

145 interval test session. No sleep was allowed during the day for the Wake group.

146 The degree of subjective sleepiness was measured by the Stanford Subjective Sleepiness

147 (SSS) scale (Hoddes et al., 1973) before each of the test sessions for both groups.

148

149 ***Experimental design for Experiment 2***

150 Subjects in Experiment 2 underwent two sleep sessions at our sleep laboratory,

151 adaptation and main experimental sleep sessions. The adaptation session was conducted prior to

152 the main experimental sleep session for the following reason. It has been shown that when

153 subjects sleep in a sleep laboratory for the first time, the sleep quality is degraded due to the new

154 environment, termed the first-night effect (FNE) (Agnew et al., 1966; Carskadon and Dement,

155 1981; Tamaki et al., 2005; Tamaki et al., 2016). To mitigate the FNE, an adaptation sleep session

156 was necessary prior to the main experimental sleep session. During the adaptation sleep session,

157 all electrodes were attached to the subjects for polysomnography (PSG) measurement. The

158 subjects slept in the same fashion as in the experimental sleep session. The adaptation session

159 was conducted approximately a week before the main experimental sleep session so that any

160 effects due to sleeping during the adaptation sleep session would not carry over to the

161 experimental sleep session.

162 On the day of the main experimental sleep session, the subjects arrived at the

163 experimental room approximately at noon (**Figure 1B, Nap group**). Then, electrodes were

164 attached for PSG measurement (see ***PSG measurement***) for which it took about an hour. After

165 the electrodes were attached, behavioral task sessions were conducted in the same way as in

166 Experiment 1. After the introductory session in which we explained how to perform the task, the

167 subjects conducted a pre-training test session of the task to measure their initial performance

168 level before training (~5 min). After the pre-training test session, the subjects underwent

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169   intensive training on the task (~ 45 min). After the training session, the post-training test session

170   (~5 min) was conducted to measure performance changes by training. There were approximately

171   2-min short breaks between the pre-training test and training sessions, as well as between the

172   training and post-training test sessions.

173   Shortly after the completion of the post-training test session, room lights were turned off

174   and the sleep session began at approximately 2 pm, lasting 90 min. This lights-off time being

175   about 2 pm was chosen to take advantage of the effect known as "mid-afternoon dip", which

176   should facilitate the onset of sleep even in subjects who do not customarily nap (Monk et al.,

177   1996; Horikawa et al., 2013; Tamaki et al., 2016). During the sleep session, PSG was measured

178   (see ***PSG measurement***). Immediately after the sleep session, a questionnaire was administered

179   to collect data about subjects' introspection regarding the nap (Tamaki et al., 2016). There was a

180   30 min break after the sleep session to reduce the sleep inertia, which is a prolonged sleepiness

181   upon waking, known to impair performance (Lubin et al., 1976). After the 30-min break, a post-

182   sleep test session (~ 5 min) was conducted to measure the changes in performance over the sleep

183   session.

184   Subjective and behavioral sleepiness (SSS (Hoddes et al., 1973), and PVT (Dinges and

185   Powell, 1985), respectively) were measured three times prior to each test session (see ***Sleepiness***

186   ***measurement***).

187   To collect data about subjects' sleep habit and handedness, 3 types of questionnaires were

188   administered prior to an adaptation sleep session. They were the Pittsburg Sleep Quality Index

189   questionnaire (PSQI; (Buysse et al., 1989)), the Morningness-Eveningness Questionnaire (MEQ;

190   (Horne and Ostberg, 1976)), and the Edinburgh Handedness Questionnaire (Oldfield, 1971).

191   Using the PSQI, we measured the following parameters: Habitual sleep quality (%), obtained by

192   [(Number of hours slept / Number of hours spent in bed) x 100], the average bedtime, wake-up

193   time, and subjective sleep-onset latency, and the global PSQI score. The global PSQI score

194   indicates the quality of subjects' habitual sleep (range: 0-21, a global score of >5 suggests poor

195   sleep). The MEQ estimates individual circadian variations. All the subjects in Experiment 2 were

196   right-handed according to the answer in the handedness questionnaire.

197

198   ***Orientation detection task***

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199   A Gabor patch was used for the orientation detection task (**Fig. 1C**). The diameter of the

200   Gabor patch was 10 degrees, presented at the center of the screen. The spatial frequency of the

201   Gabor patch was 1 cycle per degree, and the Gaussian filter sigma was 2.5 degrees. Gabor

202   patches were spatially masked by a noise pattern that was generated from a sinusoidal luminance

203   distribution at a given SNR (Shibata et al., 2017). The average luminance of the stimulus was

204   130.7 ± 3.28 cd/m^2.

205   Subjects performed the orientation detection task with a two-interval forced choice

206   (2IFC) as in previous studies (Xiao et al., 2008; Shibata et al., 2017). Subjects were presented

207   with two types of displays. One display contained a Gaussian windowed sinusoidal grating

208   (Gabor) patch with a certain signal-to-noise ratio (SNR). The other display had only noise (0%

209   SNR). Each trial started with a 500-ms fixation interval. Two displays were presented

210   sequentially for 92 ms, with a 600-ms inter-stimulus-interval (Xiao et al., 2008; Zhang et al.,

211   2010). After the two displays were presented, subjects were asked to report which display (the

212   first or the second) contained stripes, by pressing the '1' or '2' button on a keyboard.

213   The threshold SNR was measured for each orientation. The initial SNR was set to 25%.

214   The step size of the staircase was 0.03 log units to adjust the SNR with a 2-down 1-up staircase

215   procedure, which yields about 70% accuracy. The temporal order of the two displays (a Gabor

216   patch + noise or noise alone) was randomly determined in each trial. Subjects were instructed to

217   fixate on a white bull's eye fixation point (diameter = 1.5 degrees) throughout the display

218   presentations for each trial. No feedback on the accuracy of a response was provided.

219   The orientation of the Gabor patch was 10°, 70°, or 130°. One orientation was randomly

220   selected as the trained orientation for each subject. Another orientation was randomly selected as

221   an untrained orientation. The remaining one orientation was used for the introductory session

222   (see below). In the training session, a total of 600 trials was performed in 6 blocks (each100

223   trials) with the trained orientation. The test sessions measured the threshold SNR for the trained

224   and untrained orientations, for each of which one block of staircase was performed. Each block

225   for each orientation ended after 10 reversals, which resulted in about 40 trials per orientation.

226   The geometric mean of the last 6 reversals in each block was obtained as the threshold SNR for

227   the orientation.

228   The performance improvement (%) by training was calculated as the percent change in

229   the threshold SNR measured at the post-training test session normalized by that at the pre-

230   training test session [performance improvement at post-training: (pre-training – post-

231   training)/pre-training x 100]. The performance improvement (%) by the interval (sleep or wake)

232   was calculated at the post-interval test session relative to the post-training test session

233   [performance improvement at post-interval: (post-training – post-interval)/post-training x 100].

234   During the introductory session, we explained how to perform the 2IFC Gabor

235   orientation detection task, before the pre-training test in both Experiments 1 and 2. There were

236   approximately 20-30 trials in this session until the subjects reached a certain level of

237   performance. The orientation of the Gabor used for this session was neither trained nor untrained

238   orientation, as mentioned above. In addition, just before the post-interval test session in

239   Experiment 1 and just before the post-sleep session in Experiment 2, the second introductory

240   session was performed with approximately 10 trials to remind the subjects of what the task was.

241

242   ***PSG measurement***

243   In Experiment 2, the attachment of electrodes for polysomnogram (PSG) measurement,

244   which took approximately 45 min, was conducted prior to the first introductory session. PSG

245   consisted of EEG, electrooculogram (EOG), electromyogram (EMG), and electrocardiogram

246   (ECG). EEG was recorded at 25 scalp sites according to the 10% electrode position (Sharbrough

247   et al., 1991) using active electrodes (actiCap, Brain Products, LLC) with a standard amplifier

248   (BrainAmp Standard, Brain Products, LLC). The online reference was Fz, and it was re-

249   referenced to the average of the left (TP9) and right (TP10) mastoids after the recording.

250   Sampling frequency was 500 Hz. The impedance of active electrodes was kept below 20 kΩ. The

251   active electrodes included a new type of integrated impedance converter, which allowed them to

252   transmit the EEG signal with significantly lower levels of noise than traditional passive electrode

253   systems. The data quality with active electrodes with the impedance below 20 kΩ was as good as

254   5 kΩ using passive electrodes (Tamaki et al., 2016). The passive electrodes were used for EOG,

255   EMG, and ECG (BrainAmp ExG, Brain Products, LLC). Horizontal EOG was recorded using

256   two electrodes placed at the outer canthi of both eyes. Vertical EOG was measured using 4

257   electrodes 3 cm above and below both eyes. EMG was recorded from the mentum (chin). The

258   impedance was kept around 10 kΩ for the passive electrodes. Brain Vision Recorder software

259   (Brain Products, LLC) was used for recording. The data was filtered between 0.1 and 100 Hz.

260   PSG was recorded in a soundproof and shielded room.

261

262 ***Sleep-stage scoring and sleep parameters***

263   Based on the PSG data acquired during Experiment 2, sleep stages were scored for every

264 30-s epoch, following the standard criteria (Rechtschaffen and Kales, 1968; Iber et al., 2007) into

265 stage wakefulness (stage W), non-rapid eye movement (NREM) stage 1 sleep (stage N1), NREM

266 stage 2 sleep (stage N2), NREM stage 3 sleep (stage N3), and stage REM sleep (REM sleep).

267 Standard sleep parameters were obtained to indicate a general sleep structure for each

268 experiment to confirm that there is no abnormality in subjects' sleep structures. Sleep parameters

269 included the sleep-onset latency (SOL, the latency to the first appearance of stage N2 from the

270 lights-off), the percentage of each sleep stage, wake time after sleep onset (WASO, the total time

271 of stage W after sleep onset), sleep efficiency (SE, the total percentage spent in sleep), and the

272 time in bed (TIB, the time interval between lights-off and lights-on) (Iber et al., 2007).

273

274 ***EEG analyses***

275   A fast-Fourier transformation was applied to the EEG data in 5-sec epochs and smoothed

276 with a tapered cosine window (Nobili et al., 1999) to compute brain activities. Six epochs were

277 used to yield the averaged spectral data of 30 s. Spectral powers for sigma activity (13-16 Hz

278 frequency bands) were obtained during NREM sleep stages (from both N2 and N3). Sigma

279 activity of the trained region were obtained by averaging sigma power measured across six

280 occipital electrodes (PO3, PO7, O1, PO4, PO8, O2) that would cover early visual areas, which

281 are assumed to be involved in the Gabor orientation task according to the previous studies (Thut

282 et al., 2006; Viemose et al., 2013). We also obtained sigma activity from the control regions (P7,

283 P8) that are close to the middle temporal gyrus (or MT area) (Seeck et al., 2017). The MT area

284 was chosen as a control, because this region is unlikely to be involved in offline performance

285 gains of a Gabor orientation detection task, given that the MT area is known to be involved in

286 coherent motion perception (Newsome and Pare, 1988; Rees et al., 2000). We computed trained-

287 region specific sigma activity by subtraction of sigma activity of the control region from that of

288 the trained region.

289

290 ***Statistical analyses***

291   The α level (Type I error rate) of 0.05 was set for all statistical analyses. The Shapiro-

292   Wilk test was conducted for all the data, by which we confirmed that all the data were normally

293   distributed (all $p > 0.05$). The Levene's test was conducted to test for homogeneity of variance. It

294   was confirmed that homogeneity of variance was not violated for all the data (all $p > 0.05$). The

295   Grubbs' test was conducted to detect outliers. No outlier data was included in the results.

296   To analyze performance improvement, ANOVA was first conducted, then t-tests were

297   conducted as post-hoc tests. When a correction for multiple comparisons was necessary for

298   multiple t-tests, we controlled the false discovery rate (FDR) (Benjamini and Hochberg, 1995) to

299   be at 0.05. To obtain correlation coefficients, Pearson's correlation was used.

300   Statistical tests were conducted by SPSS (ver. 22, IBM Corp.).

301

Results

Experiment 1

304   We hypothesized that the offline performance gains occur in the Gabor orientation

305   detection task. If this was the case, then the performance improvement over the interval should

306   be larger in the sleep group than the wake group. In addition, since the Gabor orientation

307   detection task has trained-feature specificity (Shibata et al., 2017), we hypothesized that offline

308   performance gains occur with the trained orientation, not with the untrained orientation.

309   To test whether performance improvement over the interval is larger in the sleep

310   condition, and whether the improvement was specific to the trained orientation, we conducted a

311   2-way mixed-design ANOVA with Group (sleep vs. wake) and Orientation (trained vs.

312   untrained) factors on the performance improvement at the post-interval test session. The results

313   are shown in **Fig. 2**. The ANOVA indicated a significant 2-way interaction ($F(1,6)=6.51$,

314    $p=0.043$), a significant main effect of Group ($F(1,6)=12.63$, $p=0.012$) and a significant main

315   effect of Orientation ($F(1,6)=16.45$, $p=0.007$). For the trained orientation, the post-hoc tests

316   revealed that there was a significant difference in the performance improvement between the

317   sleep and wake groups but not for the untrained orientation (trained, $t(6)=4.11$, $p=0.006$, $q<0.05$,

318   FDR for 2 comparisons; untrained, $t(6)=0.04$, $p=0.967$). Furthermore, one-sample t-tests showed

319   that the performance improvement for the trained orientation at post-interval was significantly

320   different from 0 for the sleep group but not for the wake group (the sleep group, $t(3)=7.49$,

321    $p=0.005$, $q<0.05$, FDR for 4 comparisons including the following 3 one sample t-tests; the wake

322   group, $t(3)=0.14$, $p=0.897$). In contrast, the performance improvement for the untrained

323   orientation at post-interval was not significantly different from 0 for both groups (one-sample t-

324   test, sleep group: t(3)=1.74, p=0.181; wake group: t(3)=2.29, p=0.106). Thus, offline

325   performance gains were found for the Gabor orientation detection task, only with the trained

326   orientation. These results were consistent with the hypotheses.

327   We performed following control analyses to rule out the possibility the difference in the

328   offline performance between the groups was caused by some factors other than the experimental

329   manipulation.

330   First, we tested whether the initial SNR threshold level was different before training

331   between the groups. However, we did not find a significant difference between the sleep and

332   wake groups in the SNR threshold in the pre-training test session (t(6)=0.07, p=0.945).

333   Next, we tested whether the training effect was different between the sleep and wake

334   groups. A 2-way mixed model ANOVA with Group (sleep vs wake) and Orientation (trained vs

335   untrained) factors was conducted on the performance improvement at the post-training test

336   session. However, there was no significant main effect of Group (F(1,6)=0.06, p=0.811), no

337   significant main effect of Orientation (F(1,6)=0.02, p=0.899), or no significant interaction

338   between the factors (F(1,6)=0.48, p=0.514) was found. The results indicate that the effect of

339   training was not significantly different between the groups.

340   Finally, we tested whether the degree of subjective sleepiness was different between the

341   sleep and the wake groups, as the sleepiness may impact on the performance of the detection task.

342   A 2-way mixed design ANOVA with Group (sleep vs wake) and Session (pre-training, post-

343   training, post-interval) was conducted on the SSS ratings. None of the main effect of Group

344   (F(1,6)=0.17, p=0.695), Session (F(2,12)=3.17, p=0.079), or interaction between the factors

345   (F(2,12)=1.50, p=0.262) was significant.

346   These results indicate that the significant difference between the two groups in the

347   performance improvement over the interval at the post-interval test session cannot be attributed

348   to the initial performance, the effect of training, or subjective sleepiness.

349

350   **Experiment 2**

351   In Experiment 2, we tested whether offline performance gains occur with a nap in the

352   Gabor orientation detection task and investigated whether sigma activity during NREM sleep

353   was involved in offline performance gains of the task.

12

354

VPL performance

356   We first examined whether the performance on the orientation detection task was

357   improved only in the trained orientation after daytime nap. We conducted one-sample t-tests for

358   the performance changes for each of the trained and untrained orientations at the post-sleep test

359   session. The results indicated that offline performance gains occurred with the nap in the trained

360   orientation (**Fig. 3**). The performance was significantly improved for the trained orientation but

361   not for the untrained orientation (trained, $t(8) = 3.55$, $p = 0.008$, $q<0.05$, FDR for 2 comparisons;

362   untrained, $t(8) = 0.25$, $p = 0.811$). Furthermore, a paired t-test showed that the performance

363   improvement at post-sleep was significantly different between the trained and untrained

364   orientations ($t(8) = 2.79$, $p = 0.024$). Thus, offline performance gains by nap were specific to the

365   trained orientation.

366   Importantly, the difference in the performance improvement between the trained and

367   untrained orientations was not apparent until after sleep. First, there was no significant difference

368   in the initial SNR threshold between the trained vs. untrained orientations at the pre-training test

369   session before training ($t(8)=1.29$, $p=0.234$). Second, there was no significant difference in the

370   performance improvement (%) by training at the post-training test session ($t(8) = 0.65$, $p =$

371   0.531). These indicate that the performance improvement specific to the trained orientation

372   emerged only after sleep.

373   We compared the amount of offline performance gains obtained in Experiments 1 and 2.

374   There was not a significant difference in the amount of offline performance gains between the

375   experiments ($t(15)=0.14$, $p=0.887$), while the amount of the performance gains in Experiment 2

376   was smaller than that of Experiment 1. Thus, offline performance gains were not significantly

377   different between by night sleep and by a nap.

378

Sigma activity during NREM sleep and the offline performance gain

380   We tested the hypothesis that sigma activity was involved in the offline performance gain

381   of the detection task in a trained region specific manner. First, we obtained sigma activity in the

382   trained and untrained regions (see ***EEG analyses*** in **Materials and Methods** for more details

383   about regions). We tested whether sigma activity was larger in the trained than untrained regions.

384   We found a significant difference in sigma activity between the regions (paired t-test, $t(8)=4.86$,

385   p=0.001). Sigma activity was significantly larger in the trained than untrained regions. Next, we

386   tested whether trained-region specific sigma activity was correlated with the performance change

387   over sleep (from the post-training test session to the post-sleep test session, **Fig. 4**, see ***EEG***

388   ***analyses*** in **Materials and Methods**; see **Table 1** for sleep parameters for the sleep session). We

389   found a significant correlation between them (**Fig. 4**, r=0.74, p=0.024, n=9). The Grubbs' test

390   indicated that there was no outlier in the data. Thus, the result was consistent with the hypothesis

391   that sigma activity was involved in the offline performance gain of the detection task in a trained

392   region specific manner.

393   We next tested whether any macroscopic sleep variables, such as the duration of each

394   sleep stage was associated with the offline performance gain (see **Table 1** for all the sleep

395   parameters). We measured the Pearson's correlation coefficient with the performance change

396   over sleep and the durations of each of the sleep stages (W, N1, N2, N3, REM sleep). As a result,

397   none of the durations of sleep stages was significantly correlated with the offline performance

398   gain (stage W, r=-0.18, p=0.642; stage N1, r=0.31, p=0.418, stage N2, r=0.10, p=0.791; stage N3,

399   r=-0.25, p=0.517; REM sleep, r=0.49, p=0.181, without multiple corrections).

400   We calculated other sleep parameters such as sleep-onset latency (SOL, from the lights-

401   off to sleep onset time (min)), sleep efficiency (SE, the total sleep time divided by the time in

402   bed x 100 (%)), wake time after sleep onset (WASO, min), and total time in bed (TIB (min))

403   shown in **Table 1**. We tested whether these parameters explain the offline performance gains by

404   calculating correlation coefficients. However, none of them was significantly correlated with the

405   offline performance gains (SOL, r=0.23, p=0.551; SE r=0.18, p=0.645; WASO, r=-0.35,

406   p=0.350; TIB, r=0.17, p=0.669).

407

Quality of habitual sleep and circadian variations

408

409   The sleep quality in Experiment 2 was relatively poorer than our recent studies (Bang et

410   al., 2014; Tamaki et al., 2016). The sleep efficiency (%) during the sleep session in the sleep

411   group was 73.6% (**Table 1**). In contrast, in our previous study, the sleep efficiency was about

412   88.7%-92.8% (Bang et al., 2014; Tamaki et al., 2016) in a sleep session which was done after the

413   adaptation session to eliminate the FNE (Tamaki et al., 2016) (see ***Experimental design for***

414   ***Experiment 2*** in **Materials and Methods** for more information on the FNE). In a similar vein,

415   the WASO in the present study (14.2 min) seems longer compared to the previous studies where

416   it was only 1 - 4.18 min (Bang et al., 2014; Tamaki et al., 2016).

417   This made us wonder whether the subjects in Experiment 2 were actually poor sleepers,

418   and/or whether they were extreme morning- or evening types. Thus, we analyzed whether the

419   quality of subjects' habitual sleep was poor using the PSQI questionnaire (Buysse et al., 1989),

420   and whether they were extreme morning or evening type using the MEQ questionnaire (Horne

421   and Ostberg, 1976). The PSQI and MEQ were administered prior to sleep sessions in Experiment

422   2 (**Table 2**).

423   PSQI assesses whether subjects have a sleep problem (Buysse et al., 1989). If the global

424   PSQI score equals or is larger than 5, this suggests that subjects have a sleep problem. However,

425   the average global PSQI score in the subjects in Experiment 2 was 2.7 ± 0.37, ranged 1-4, which

426   indicated that none of subjects was suspected of having sleep problems. In addition, based on the

427   PSQI data, we obtained the subjects' habitual bedtime, wake-up time, the average sleep-onset

428   latency, the estimated sleep duration, and the habitual sleep efficiency (**Table 2**), These scores in

429   the present subjects in Experiment 2 were considered in normal ranges (Buysse et al., 1989).

430   MEQ assesses whether the subject is a morning type or evening type (Horne and Ostberg,

431   1976). Such variations in the circadian timing may affect performance (Kerkhof, 1985). The

432   average MEQ score was 55.2 ± 2.63 with the range between 46-67, which fell into the

433   intermediate type of morningness-eveningness (neither extreme morning nor evening type)

434   (Horne and Ostberg, 1976). These results confirmed that none of the subjects had sleep problems

435   or was of extreme morning or evening type, suggesting that all the subjects had normal sleep-

436   wake habits and were all good sleepers.

437   We next examined whether any of the measures of sleep habits or habitual sleep quality

438   were related to the performance change. We measured the Pearson's correlation coefficient

439   between the offline performance gain over sleep and the habitual sleep efficiency, the habitual

440   sleep duration, the global PSQI score, and MEQ score. None of these showed a significant

441   correlation with the offline performance gain (the habitual sleep duration, $r=0.54$, $p=0.134$; the

442   habitual sleep efficiency, $r=0.52$, $p=0.150$; the global PSQI score, $r=0.12$, $p=0.763$; the MEQ

443   score, $r=-0.66$, $p=0.052$, without correction for multiple comparisons).

444

445   **Discussion**

15

446   The present results demonstrated that the offline performance gain occurred with a Gabor

447   orientation detection task by nocturnal sleep as well as a daytime nap, in a trained-feature

448   specific manner. Most of the previous studies, which tested offline performance gains in VPL

449   used a discrimination task, in particular, TDT. However, the present study clearly showed that

450   offline performance gains occur with a Gabor orientation detection task. This indicates that

451   offline performance gains are not specific to a discrimination task in VPL.

452   We found that regional sigma activity in early visual areas was significantly correlated

453   with performance change on the orientation detection task between before and after sleep. It was

454   shown that sigma activity was involved in the offline performance gain of a different task (TDT)

455   over sleep (Bang et al., 2014). Thus, it is possible that offline performance gain is commonly

456   associated with regional sigma activity during sleep in visual areas for VPL.

457   Sigma activity corresponds to the activities of sleep spindles, which are associated with

458   various types of learning, including learning on declarative and procedural motor tasks (Gais et

459   al., 2002; Schabus et al., 2004; Clemens et al., 2006; Fogel and Smith, 2006; Nishida and Walker,

460   2007; Tamminen et al., 2010; Tamaki et al., 2013; Laventure et al., 2016; Antony et al., 2018;

461   Boutin et al., 2018). Sleep spindles are specific waves used for sleep stage scoring and appear

462   around the central region during NREM sleep (Rechtschaffen and Kales, 1968; Iber et al., 2007).

463   In the present study, because early visual areas were the targeted regions for offline performance

464   gains of VPL over sleep, we extracted the strength of sigma activity that corresponds to the

465   frequency of sleep spindles from early visual areas. The precise causal relationship between

466   sigma activity and learning are yet to be clarified. However, it has been shown that stimulation

467   whose frequency corresponded to sleep spindles increases long-term potentiation (Rosanova and

468   Ulrich, 2005). Thus, the present results support the idea that regional sigma activity in early

469   visual areas plays a crucial role in offline performance gains of VPL, possibly by increasing

470   regional plasticity in early visual areas during NREM sleep.

471   The general sleep quality, as indicated in the sleep efficiency and wake time after sleep

472   onset in Experiment 2 seemed to be lower in the present study in comparison to our previous

473   studies (Bang et al., 2014; Tamaki et al., 2016). Although this is beyond the scope of the present

474   study, we speculate that it might be caused by the light exposure from the display of the current

475   stimulus. It has been shown that light exposures before sleep lower the sleep quality and cause

476   more arousals during sleep (Czeisler et al., 1986; Czeisler et al., 1990; Khalsa et al., 2003). As

477   such, it has been shown that playing a computer game with a bright display worsens the sleep

478   quality (Higuchi et al., 2005). In one of our previous studies, which used TDT, the sleep

479   efficiency was about 90% (Bang et al., 2014) while the sleep efficiency was 74.6% in the present

480   study. We measured the luminance for these stimuli. Interestingly, the average luminance for one

481   trial of the Gabor orientation detection task used in the present study was 130.7 ± 3.28 cd/m^2,

482   whereas that of TDT was only 0.4 ± 0.07 cd/m^2. Thus, the current visual stimulus was much

483   brighter than the previous one, as the average luminance of the used visual stimuli was much

484   higher in the present than previous studies (Bang et al., 2014) . We speculate that this may be the

485   trigger for the relatively lower quality of sleep in the present study, as other factors, which are

486   known to influence the quality of sleep was controlled and matched between studies including

487   the FNE (Agnew et al., 1966; Carskadon and Dement, 1981; Tamaki et al., 2005; Tamaki et al.,

488   2016), age (Dijk et al., 2000) and habitual sleep problems (Buysse et al., 1989; Breslau et al.,

489   1996; Morin et al., 1999; Morin et al., 2006). In addition, according to the PSQI and MEQ

490   questionnaires, they were of good sleepers and intermediate morningness-eveningness types

491   (Horne and Ostberg, 1976). Thus, only the brightness of the visual stimulus may account for the

492   relatively lower quality of sleep in the present study.

493   However, it is important to note that the lower quality of sleep was not correlated with

494   performance improvement over sleep in Experiment 2. None of sleep efficiency, wake time after

495   sleep onset, sleep-onset latency and time in bed was correlated with performance improvement.

496   If the wake time during the sleep session was the cause of offline performance gains, there

497   should have been a good correlation for each parameter with offline performance gains. In

498   addition, the results of Experiment 1 clearly showed that the interval that contained sleep led to

499   performance improvements, while the interval that included only wakefulness did not lead to

500   performance improvements. These results altogether demonstrate that offline performance gains

501   of an orientation detection task are a sleep-state dependent process.

502   In conclusion, the present study demonstrates that offline performance gains were found

503   after training on an orientation detection task. This indicates that offline performance gains are

504   not limited to discrimination tasks including TDT. The present results also suggest that regional

505   sigma activity plays a certain role in facilitation of VPL during sleep.

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515   **Author Contributions**

516   M.T. and Y.S. designed the research. M.T. and Z.W. performed the experiments and analyzed

517   the data. M.T., T.W., and Y.S. wrote the manuscript.

518

519   **Conflict of Interest**

520   The authors declare no conflict of interest.

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References

Agnew, H.W., Jr., Webb, W.B., and Williams, R.L. (1966). The first night effect: an EEG study of sleep. *Psychophysiology* 2(3)**,** 263-266. doi: 10.1111/j.1469-8986.1966.tb02650.x

Antony, J.W., Piloto, L., Wang, M., Pacheco, P., Norman, K.A., and Paller, K.A. (2018). Sleep Spindle Refractoriness Segregates Periods of Memory Reactivation. *Curr Biol* 28(11)**,** 1736-1743 e1734. doi: 10.1016/j.cub.2018.04.020.

Bang, J.W., Khalilzadeh, O., Hamalainen, M., Watanabe, T., and Sasaki, Y. (2014). Location specific sleep spindle activity in the early visual areas and perceptual learning. *Vision Res* 99**,** 162-171. doi: 10.1016/j.visres.2013.12.014.

Benjamini, Y., and Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J. R. Stat. Soc. Ser. B Stat. Methodol.* 57(1)**,** 289-300.

Berard, A.V., Cain, M.S., Watanabe, T., and Sasaki, Y. (2015). Frequent video game players resist perceptual interference. *PLoS One* 10(3)**,** e0120011. doi: 10.1371/journal.pone.0120011.

Born, J., and Wilhelm, I. (2012). System consolidation of memory during sleep. *Psychol Res* 76(2)**,** 192-203. doi: 10.1007/s00426-011-0335-6.

Boutin, A., Pinsard, B., Bore, A., Carrier, J., Fogel, S.M., and Doyon, J. (2018). Transient synchronization of hippocampo-striato-thalamo-cortical networks during sleep spindle oscillations induces motor memory consolidation. *Neuroimage* 169**,** 419-430. doi: 10.1016/j.neuroimage.2017.12.066.

Breslau, N., Roth, T., Rosenthal, L., and Andreski, P. (1996). Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry* 39(6)**,** 411-418.

Bridwell, D.A., Hecker, E.A., Serences, J.T., and Srinivasan, R. (2013). Individual differences in attention strategies during detection, fine discrimination, and coarse discrimination. *J Neurophysiol* 110(3)**,** 784-794. doi: 10.1152/jn.00520.2012.

Buysse, D.J., Reynolds, C.F., 3rd, Monk, T.H., Berman, S.R., and Kupfer, D.J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 28(2)**,** 193-213.

Carskadon, M.A., and Dement, W.C. (1981). Cumulative effects of sleep restriction on daytime sleepiness. *Psychophysiology* 18(2)**,** 107-113. doi: 10.1111/j.1469-8986.1981.tb02921.x

Censor, N., Karni, A., and Sagi, D. (2006). A link between perceptual learning, adaptation and sleep. *Vision Res* 46(23)**,** 4071-4074. doi: 10.1016/j.visres.2006.07.022.

Clemens, Z., Fabo, D., and Halasz, P. (2006). Twenty-four hours retention of visuospatial memory correlates with the number of parietal sleep spindles. *Neurosci Lett* 403(1-2)**,** 52-56. doi: 10.1016/j.neulet.2006.04.035.

Czeisler, C.A., Allan, J.S., Strogatz, S.H., Ronda, J.M., Sanchez, R., Rios, C.D., et al. (1986). Bright light resets the human circadian pacemaker independent of the timing of the sleep-wake cycle. *Science* 233(4764)**,** 667-671.

Czeisler, C.A., Johnson, M.P., Duffy, J.F., Brown, E.N., Ronda, J.M., and Kronauer, R.E. (1990). Exposure to bright light and darkness to treat physiologic maladaptation to night work. *N Engl J Med* 322(18)**,** 1253-1259. doi: 10.1056/NEJM199005033221801.

Diekelmann, S., and Born, J. (2010). The memory function of sleep. *Nat Rev Neurosci* 11(2)**,** 114-126. doi: 10.1038/nrn2762.

567   Dijk, D.J., Duffy, J.F., and Czeisler, C.A. (2000). Contribution of circadian physiology and sleep
568   homeostasis to age-related changes in human sleep. *Chronobiol Int* 17(3)**,** 285-311.
569   Dinges, D.F., and Powell, J.W. (1985). Microcomputer analyses of performance on a portable,
570   simple visual RT task during sustained operations. *Behavior Research Methods,*
571   *Instruments, & Computers* 17(6)**,** 652-655. doi: 10.3758/bf03200977.
572   Fogel, S.M., and Smith, C.T. (2006). Learning-dependent changes in sleep spindles and Stage 2
573   sleep. *J Sleep Res* 15(3)**,** 250-255. doi: 10.1111/j.1365-2869.2006.00522.x.
574   Gais, S., Molle, M., Helms, K., and Born, J. (2002). Learning-dependent increases in sleep
575   spindle density. *J Neurosci* 22(15)**,** 6830-6834. doi: 20026697.
576   Gais, S., Plihal, W., Wagner, U., and Born, J. (2000). Early sleep triggers memory for early
577   visual discrimination skills. *Nat Neurosci* 3(12)**,** 1335-1339. doi: 10.1038/81881.
578   Green, C.S., and Bavelier, D. (2003). Action video game modifies visual selective attention.
579   *Nature* 423(6939)**,** 534-537. doi: 10.1038/nature01647.
580   Higuchi, S., Motohashi, Y., Liu, Y., and Maeda, A. (2005). Effects of playing a computer game
581   using a bright display on presleep physiological variables, sleep latency, slow wave sleep
582   and REM sleep. *J Sleep Res* 14(3)**,** 267-273. doi: 10.1111/j.1365-2869.2005.00463.x.
583   Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., and Dement, W.C. (1973). Quantification of
584   sleepiness: a new approach. *Psychophysiology* 10(4)**,** 431-436. doi: 10.1111/j.1469-
585   8986.1973.tb00801.x.
586   Horikawa, T., Tamaki, M., Miyawaki, Y., and Kamitani, Y. (2013). Neural decoding of visual
587   imagery during sleep. *Science* 340(6132)**,** 639-642. doi: 10.1126/science.1234330.
588   Horne, J.A., and Ostberg, O. (1976). A self-assessment questionnaire to determine morningness-
589   eveningness in human circadian rhythms. *Int J Chronobiol* 4(2)**,** 97-110.
590   Huber, R., Ghilardi, M.F., Massimini, M., and Tononi, G. (2004). Local sleep and learning.
591   *Nature* 430(6995)**,** 78-81.
592   Iber, C., Ancoli-Israel, S., Chesson, A., and Quan, S.F. (2007). *The AASM manual for the*
593   *scoring of sleep and associated events: rules, terminology, and technical specification.*
594   Westchester, IL: American Academy of Sleep Medicine.
595   Jazayeri, M., and Movshon, J.A. (2006). Optimal representation of sensory information by neural
596   populations. *Nat Neurosci* 9(5)**,** 690-696. doi: 10.1038/nn1691.
597   Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M.M., Turner, R., et al. (1998). The
598   acquisition of skilled motor performance: fast and slow experience-driven changes in
599   primary motor cortex. *Proc Natl Acad Sci U S A* 95(3)**,** 861-868.
600   Karni, A., and Sagi, D. (1991). Where practice makes perfect in texture discrimination: evidence
601   for primary visual cortex plasticity. *Proc Natl Acad Sci U S A* 88(11)**,** 4966-4970. doi:
602   10.1073/pnas.88.11.4966.
603   Karni, A., Tanne, D., Rubenstein, B.S., Askenasy, J.J., and Sagi, D. (1994). Dependence on
604   REM sleep of overnight improvement of a perceptual skill. *Science* 265(5172)**,** 679-682.
605   doi: 10.1126/science.8036518.
606   Kerkhof, G.A. (1985). Inter-individual differences in the human circadian system: a review. *Biol*
607   *Psychol* 20(2)**,** 83-112.
608   Khalsa, S.B., Jewett, M.E., Cajochen, C., and Czeisler, C.A. (2003). A phase response curve to
609   single bright light pulses in human subjects. *J Physiol* 549(Pt 3)**,** 945-952. doi:
610   10.1113/jphysiol.2003.040477.

20

611   Laureys, S., Peigneux, P., Phillips, C., Fuchs, S., Degueldre, C., Aerts, J., et al. (2001).
612   Experience-dependent changes in cerebral functional connectivity during human rapid
613   eye movement sleep. *Neuroscience* 105(3)**,** 521-525.
614   Laventure, S., Fogel, S., Lungu, O., Albouy, G., Sevigny-Dupont, P., Vien, C., et al. (2016).
615   NREM2 and Sleep Spindles Are Instrumental to the Consolidation of Motor Sequence
616   Memories. *PLoS Biol* 14(3)**,** e1002429. doi: 10.1371/journal.pbio.1002429.
617   Laventure, S., Pinsard, B., Lungu, O., Carrier, J., Fogel, S., Benali, H., et al. (2018). Beyond
618   spindles: interactions between sleep spindles and boundary frequencies during cued
619   reactivation of motor memory representations. *Sleep* zsy142. doi:
620   https://doi.org/10.1093/sleep/zsy142.
621   Law, C.T., and Gold, J.I. (2008). Neural correlates of perceptual learning in a sensory-motor, but
622   not a sensory, cortical area. *Nat Neurosci* 11(4)**,** 505-513. doi: 10.1038/nn2070.
623   Li, R., Polat, U., Makous, W., and Bavelier, D. (2009). Enhancing the contrast sensitivity
624   function through action video game training. *Nat Neurosci* 12(5)**,** 549-551. doi:
625   10.1038/nn.2296.
626   Lu, Z.L., Hua, T., Huang, C.B., Zhou, Y., and Dosher, B.A. (2011). Visual perceptual learning.
627   *Neurobiol Learn Mem* 95(2)**,** 145-151. doi: 10.1016/j.nlm.2010.09.010.
628   Lubin, A., Hord, D.J., Tracy, M.L., and Johnson, L.C. (1976). Effects of exercise, bedrest and
629   napping on performance decrement during 40 hours. *Psychophysiology* 13(4)**,** 334-339.
630   doi: 10.1111/j.1469-8986.1976.tb03086.x.
631   Manoach, D.S., Pan, J.Q., Purcell, S.M., and Stickgold, R. (2016). Reduced Sleep Spindles in
632   Schizophrenia: A Treatable Endophenotype That Links Risk Genes to Impaired
633   Cognition? *Biol Psychiatry* 80(8)**,** 599-608. doi: 10.1016/j.biopsych.2015.10.003.
634   Manoach, D.S., and Stickgold, R. (2009). Does abnormal sleep impair memory consolidation in
635   schizophrenia? *Front Hum Neurosci* 3**,** 21. doi: 10.3389/neuro.09.021.2009.
636   Manoach, D.S., Thakkar, K.N., Stroynowski, E., Ely, A., McKinley, S.K., Wamsley, E., et al.
637   (2010). Reduced overnight consolidation of procedural learning in chronic medicated
638   schizophrenia is related to specific sleep stages. *J Psychiatr Res* 44(2)**,** 112-120. doi:
639   10.1016/j.jpsychires.2009.06.011.
640   Maquet, P., Laureys, S., Peigneux, P., Fuchs, S., Petiau, C., Phillips, C., et al. (2000).
641   Experience-dependent changes in cerebral activation during human REM sleep. *Nat
642   Neurosci* 3(8)**,** 831-836. doi: 10.1038/77744.
643   Mascetti, L., Muto, V., Matarazzo, L., Foret, A., Ziegler, E., Albouy, G., et al. (2013). The
644   impact of visual perceptual learning on sleep and local slow-wave initiation. *J Neurosci*
645   33(8)**,** 3323-3331. doi: 10.1523/JNEUROSCI.0763-12.2013.
646   Matarazzo, L., Franko, E., Maquet, P., and Vogels, R. (2008). Offline processing of memories
647   induced by perceptual visual learning during subsequent wakefulness and sleep: A
648   behavioral study. *J Vis* 8(4)**,** 7 1-9. doi: 10.1167/8.4.7.
649   McDevitt, E.A., Rokem, A., Silver, M.A., and Mednick, S.C. (2014). Sex differences in sleep-
650   dependent perceptual learning. *Vision Res* 99**,** 172-179. doi: 10.1016/j.visres.2013.10.009.
651   Mednick, S., Nakayama, K., and Stickgold, R. (2003). Sleep-dependent learning: a nap is as
652   good as a night. *Nat Neurosci* 6(7)**,** 697-698. doi: 10.1038/nn1078.
653   Monk, T.H., Buysse, D.J., Reynolds, C.F., 3rd, and Kupfer, D.J. (1996). Circadian determinants
654   of the postlunch dip in performance. *Chronobiol Int* 13(2)**,** 123-133. doi:
655   10.3109/07420529609037076

656   Morin, C.M., Bootzin, R.R., Buysse, D.J., Edinger, J.D., Espie, C.A., and Lichstein, K.L. (2006).
657   Psychological and behavioral treatment of insomnia:update of the recent evidence (1998-
658   2004). *Sleep* 29(11)**,** 1398-1414.
659   Morin, C.M., Hauri, P.J., Espie, C.A., Spielman, A.J., Buysse, D.J., and Bootzin, R.R. (1999).
660   Nonpharmacologic treatment of chronic insomnia. An American Academy of Sleep
661   Medicine review. *Sleep* 22(8)**,** 1134-1156.
662   Newsome, W.T., and Pare, E.B. (1988). A selective impairment of motion perception following
663   lesions of the middle temporal visual area (MT). *J Neurosci* 8(6)**,** 2201-2211.
664   Nishida, M., and Walker, M.P. (2007). Daytime naps, motor memory consolidation and
665   regionally specific sleep spindles. *PLoS One* 2(4)**,** e341. doi:
666   10.1371/journal.pone.0000341.
667   Nobili, L., Baglietto, M.G., De Carli, F., Savoini, M., Schiavi, G., Zanotto, E., et al. (1999). A
668   quantified analysis of sleep electroencephalography in anorectic adolescents. *Biol*
669   *Psychiatry* 45(6)**,** 771-775. doi: 10.1016/s0006-3223(98)00107-3.
670   Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh inventory.
671   *Neuropsychologia* 9(1)**,** 97-113.
672   Rasch, B., and Born, J. (2013). About sleep's role in memory. *Physiol Rev* 93(2)**,** 681-766. doi:
673   10.1152/physrev.00032.2012.
674   Rechtschaffen, A., and Kales, A. (1968). *A Manual of Standardized Terminology, Techniques,*
675   *and Scoring System for Sleep Stages of Human Subjects.* Washington, DC: Public Health
676   Service, US Government Printing Office.
677   Rees, G., Friston, K., and Koch, C. (2000). A direct quantitative relationship between the
678   functional properties of human and macaque V5. *Nat Neurosci* 3(7)**,** 716-723. doi:
679   10.1038/76673.
680   Regan, D., and Beverley, K.I. (1985). Postadaptation orientation discrimination. *J Opt Soc Am A*
681   2(2)**,** 147-155.
682   Rosanova, M., and Ulrich, D. (2005). Pattern-specific associative long-term potentiation induced
683   by a sleep spindle-related spike train. *J Neurosci* 25(41)**,** 9398-9405. doi:
684   10.1523/JNEUROSCI.2149-05.2005.
685   Sagi, D. (2011). Perceptual learning in Vision Research. *Vision Res* 51(13)**,** 1552-1566. doi:
686   10.1016/j.visres.2010.10.019.
687   Sasaki, Y., Nanez, J.E., and Watanabe, T. (2010). Advances in visual perceptual learning and
688   plasticity. *Nat Rev Neurosci* 11(1)**,** 53-60. doi: 10.1038/nrn2737.
689   Schabus, M., Gruber, G., Parapatics, S., Sauter, C., Klosch, G., Anderer, P., et al. (2004). Sleep
690   spindles and their significance for declarative memory consolidation. *Sleep* 27(8)**,** 1479-
691   1485.
692   Schoups, A., Vogels, R., Qian, N., and Orban, G. (2001). Practising orientation identification
693   improves orientation coding in V1 neurons. *Nature* 412(6846)**,** 549-553.
694   Schwartz, S., Maquet, P., and Frith, C. (2002). Neural correlates of perceptual learning: a
695   functional MRI study of visual texture discrimination. *Proc Natl Acad Sci U S A* 99(26)**,**
696   17137-17142. doi: 10.1073/pnas.242414599.
697   Seeck, M., Koessler, L., Bast, T., Leijten, F., Michel, C., Baumgartner, C., et al. (2017). The
698   standardized EEG electrode array of the IFCN. *Clin Neurophysiol* 128(10)**,** 2070-2077.
699   doi: 10.1016/j.clinph.2017.06.254.

700 Seitz, A.R., Yamagishi, N., Werner, B., Goda, N., Kawato, M., and Watanabe, T. (2005). Task-
701   specific disruption of perceptual learning. *Proc Natl Acad Sci U S A* 102(41)**,** 14895-
702   14900. doi: 10.1073/pnas.0505765102.
703 Sejnowski, T.J., and Destexhe, A. (2000). Why do we sleep? *Brain Res* 886(1-2)**,** 208-223. doi:
704   10.1016/s0006-8993(00)03007-9
705 Sharbrough, F.C.G.E., Lesser, R.P., Lüders, H., Nuwer, M., and Picton, T.W. (1991). American
706   electroencephalographic society guidelines for standard electrode position nomenclature.
707   *J. Clin. Neurophysiol.* 8(2)**,** 200-202.
708 Shibata, K., Sasaki, Y., Bang, J.W., Walsh, E.G., Machizawa, M.G., Tamaki, M., et al. (2017).
709   Overlearning hyperstabilizes a skill by rapidly making neurochemical processing
710   inhibitory-dominant. *Nat Neurosci* 20(3)**,** 470-475. doi: 10.1038/nn.4490.
711 Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature* 437(7063)**,** 1272-1278.
712   doi: 10.1038/nature04286.
713 Stickgold, R., James, L., and Hobson, J.A. (2000a). Visual discrimination learning requires sleep
714   after training. *Nat Neurosci* 3(12)**,** 1237-1238. doi: 10.1038/81756.
715 Stickgold, R., Whidbee, D., Schirmer, B., Patel, V., and Hobson, J.A. (2000b). Visual
716   discrimination task improvement: A multi-step process occurring during sleep. *J Cogn
717   Neurosci* 12(2)**,** 246-254. doi: 10.1162/089892900562075.
718 Tamaki, M., Bang, J.W., Watanabe, T., and Sasaki, Y. (2014). The first-night effect suppresses
719   the strength of slow-wave activity originating in the visual areas during sleep. *Vision Res*
720   99**,** 154-161. doi: 10.1016/j.visres.2013.10.023.
721 Tamaki, M., Bang, J.W., Watanabe, T., and Sasaki, Y. (2016). Night watch in one brain
722   hemisphere during sleep associated with the first-night effect in humans. *Curr Biol* 26(9)**,**
723   1190-1194. doi: 10.1016/j.cub.2016.02.063.
724 Tamaki, M., Huang, T.R., Yotsumoto, Y., Hamalainen, M., Lin, F.H., Nanez, J.E., Sr., et al.
725   (2013). Enhanced spontaneous oscillations in the supplementary motor area are
726   associated with sleep-dependent offline learning of finger-tapping motor-sequence task. *J
727   Neurosci* 33(34)**,** 13894-13902. doi: 10.1523/JNEUROSCI.1198-13.2013.
728 Tamaki, M., Matsuoka, T., Nittono, H., and Hori, T. (2008). Fast sleep spindle (13-15 hz)
729   activity correlates with sleep-dependent improvement in visuomotor performance. *Sleep*
730   31(2)**,** 204-211.
731 Tamaki, M., Nittono, H., Hayashi, M., and Hori, T. (2005). Examination of the first-night effect
732   during the sleep-onset period. *Sleep* 28(2)**,** 195-202.
733 Tamminen, J., Payne, J.D., Stickgold, R., Wamsley, E.J., and Gaskell, M.G. (2010). Sleep
734   spindle activity is associated with the integration of new memories and existing
735   knowledge. *J Neurosci* 30(43)**,** 14356-14360. doi: 10.1523/JNEUROSCI.3028-10.2010.
736 Thut, G., Nietzel, A., Brandt, S.A., and Pascual-Leone, A. (2006). Alpha-band
737   electroencephalographic activity over occipital cortex indexes visuospatial attention bias
738   and predicts visual target detection. *J Neurosci* 26(37)**,** 9494-9502. doi:
739   10.1523/JNEUROSCI.0875-06.2006.
740 Tononi, G., and Cirelli, C. (2014). Sleep and the price of plasticity: from synaptic and cellular
741   homeostasis to memory consolidation and integration. *Neuron* 81(1)**,** 12-34. doi:
742   10.1016/j.neuron.2013.12.025.
743 Viemose, I., Moller, P., Laugesen, J.L., Schachtman, T.R., Manoharan, T., and Christoffersen,
744   G.R. (2013). Appetitive long-term taste conditioning enhances human visually evoked
745   EEG responses. *Behav Brain Res* 253**,** 1-8. doi: 10.1016/j.bbr.2013.06.033.

746 Walker, M.P. (2005). A refined model of sleep and the time course of memory formation. *Behav*
747   *Brain Sci* 28(1)**,** 51-64; discussion 64-104.
748 Walker, M.P., Brakefield, T., Morgan, A., Hobson, J.A., and Stickgold, R. (2002). Practice with
749   sleep makes perfect: sleep-dependent motor skill learning. *Neuron* 35(1)**,** 205-211. doi:
750   10.1016/s0896-6273(02)00746-8.
751 Walker, M.P., and Stickgold, R. (2005). It's practice, with sleep, that makes perfect: implications
752   of sleep-dependent learning and plasticity for skill performance. *Clin Sports Med* 24(2)**,**
753   301-317, ix. doi: 10.1016/j.csm.2004.11.002.
754 Walker, M.P., Stickgold, R., Jolesz, F.A., and Yoo, S.S. (2005). The functional anatomy of
755   sleep-dependent visual skill learning. *Cereb Cortex* 15(11)**,** 1666-1675. doi:
756   10.1093/cercor/bhi043.
757 Xiao, L.Q., Zhang, J.Y., Wang, R., Klein, S.A., Levi, D.M., and Yu, C. (2008). Complete
758   transfer of perceptual learning across retinal locations enabled by double training. *Curr*
759   *Biol* 18(24)**,** 1922-1926. doi: 10.1016/j.cub.2008.10.030.
760 Yotsumoto, Y., Chang, L.H., Watanabe, T., and Sasaki, Y. (2009a). Interference and feature
761   specificity in visual perceptual learning. *Vision Res* 49(21)**,** 2611-2623. doi:
762   10.1016/j.visres.2009.08.001.
763 Yotsumoto, Y., Sasaki, Y., Chan, P., Vasios, C.E., Bonmassar, G., Ito, N., et al. (2009b).
764   Location-specific cortical activation changes during sleep after training for perceptual
765   learning. *Curr Biol* 19(15)**,** 1278-1282. doi: 10.1016/j.cub.2009.06.011.
766 Zhang, J.Y., Zhang, G.L., Xiao, L.Q., Klein, S.A., Levi, D.M., and Yu, C. (2010). Rule-based
767   learning explains visual perceptual learning and its specificity and transfer. *J Neurosci*
768   30(37)**,** 12323-12328. doi: 10.1523/JNEUROSCI.0704-10.2010.
769
770
771

772 **Table legends**

773

774 **Table 1. SOL**, sleep-onset latency. **WASO**, wake time after sleep onset. **SE**, sleep efficiency.

775 **TIB**, the time in bed which indicates the duration of each sleep session (the time interval

776 between lights-off and lights-on)

777

778 **Table 2.** The MEQ score was measured by the Morningness-Eveningness Questionnaire (MEQ).

779 Other parameters were measured using the Pittsburg Sleep Quality Index questionnaire (PSQI).

780

781

Table 1. Sleep parameters for Experiment 2

	Mean ± SEM		
Stage W (min)	21.4	±	5.61
Stage N1 (min)	11.2	±	2.45
Stage N2 (min)	25.3	±	4.03
Stage N3 (min)	18.0	±	5.30
REM sleep (min)	5.4	±	2.61
SOL (min)	11.0	±	3.84
WASO (min)	14.2	±	4.76
SE (%)	73.6	±	7.45
TIB (min)	85.2	±	1.96

Table 2. Habitual sleep parameters

	Mean ± SEM		
Bedtime	23:16	±	0:09
Wake-up time	7:42	±	0:16
Sleep duration	7.8	±	0.20
Sleep onset latency	11.9	±	2.57
Habitual sleep efficiency (%)	92.8	±	2.25
The global PSQI score	2.7	±	0.37
The MEQ score	55.2	±	2.63

782 **Figure legends**

783

784 **Fig. 1.** Experimental Designs and the Gabor orientation task. (**A**) Experiment 1. (**B**) Experiment

785 2. (**C**) Schematic illustration of one trial of the Gabor orientation task.

786

787 **Fig. 2.** The mean performance improvement (±SEM) at post-interval test session for the sleep

788 and the wake groups in Experiment 1. See the main text for the results of ANOVA. Asterisks

789 (**) indicate that post-hoc t-tests (one sample t-test and a paired t-test) showed significance at

790 p<.01. FDR applied (see the main text for details).

791

792 **Fig. 3.** The mean performance improvement (±SEM) at post-interval test session for Experiment

793 2. N=9. Paired and one-sample t-tests, *p<.05. See main test for more details of statistical results.

794

795 **Fig. 4.** Correlation between the offline performance gains and trained-region specific sigma

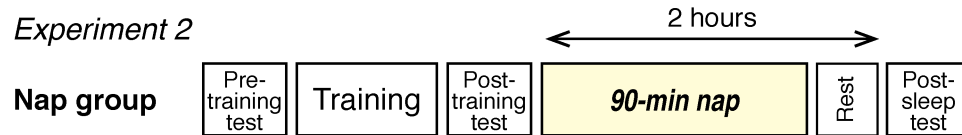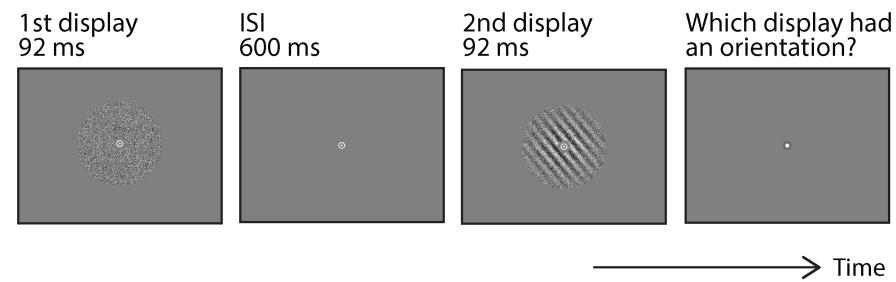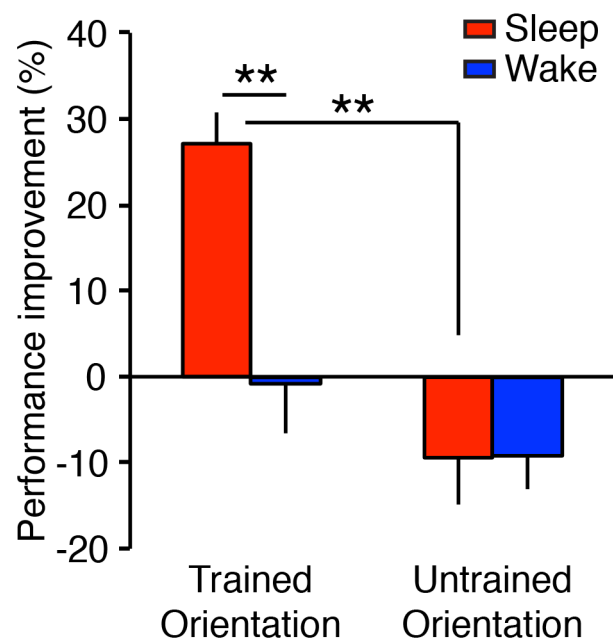796 activity during NREM sleep. N=9. **p<.01. No outliers detected by the Grubb's test.

797

Figure 1

A

Experiment 1

B

Experiment 2
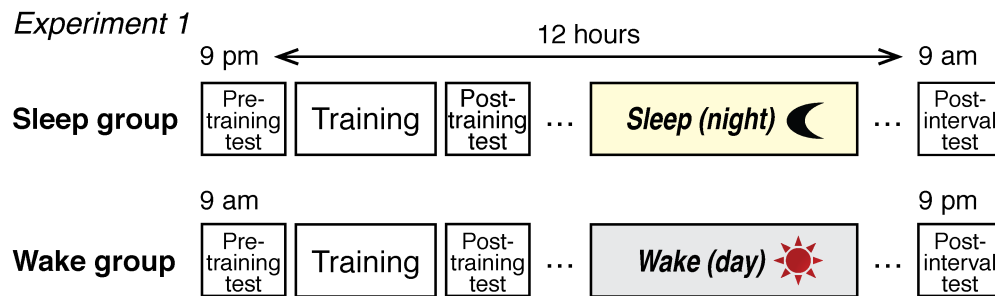
C

Figure 2

Figure 3

Figure 4