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HAL Authorization

1 **M/EEG dynamics underlying reserve, resilience and maintenance**
2 **in ageing: A review**

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20 **Abstract**

21 Cognitive reserve and resilience refer to the set of processes allowing the preservation of
22 cognitive performance in the presence of structural and functional brain changes. Investigations
23 of these concepts have provided unique insights on the heterogeneity of cognitive and brain
24 changes associated with aging. Previous work mainly relied on methods benefiting from a high
25 spatial precision but a low temporal resolution, and thus the temporal brain dynamics
26 underlying these concepts remain poorly known. Moreover, while spontaneous fluctuations of
27 neural activity have long been considered as noise, recent work highlights its critical
28 contribution to brain functions. Here, we synthesize the current state of knowledge from MEG
29 (magnetoencephalography) and EEG (electroencephalography) studies that investigated the
30 contribution of maintenance of neural synchrony, and variability of brain dynamics, to cognitive
31 changes associated with healthy aging and the progression of neurodegenerative disease (such
32 as Alzheimer disease). The reviewed findings highlight that compensations could be associated
33 with increased synchrony of higher (>10Hz) frequency bands. Maintenance of young-like
34 synchrony patterns was also observed in healthy older individuals. Both maintenance and
35 compensation appear to be highly related with preserved structural integrity (brain reserve).
36 However, increased synchrony was also found to be deleterious in some case and reflect
37 neurodegenerative processes. These results provide major elements on the stability or
38 variability of functional networks as well as maintenance of neural synchrony over time, and
39 their association with individual cognitive changes with aging. These findings could provide
40 new and interesting considerations about cognitive reserve, maintenance, and resilience of brain
41 functions and cognition.

42 *Keywords: Aging; Cognition; M/EEG; Dementia; Connectivity*

43 Introduction

44 Understanding the evolution of cognition as we age is crucial, not only because it is
45 intimately related to everyone's subjective experience, but to help describing and better
46 understanding cognition itself. Cognitive aging is a highly variable phenomenon, characterized
47 by a decline in cognitive abilities that might lead to higher risk of pathological aging in some
48 individuals, while others are able to remain efficient in most everyday tasks until an advanced
49 age (Reuter-Lorenz & Park, 2014). Research on the variability of age-related changes across
50 individuals aims at answering at several questions, such as the factors associated with preserved
51 cognitive functioning with age (the "*why*" question), or what differs between individuals with
52 preserved *versus* declined cognitive performance (the "*how*" question). While lifestyle activities
53 associated with reduced risk of cognitive decline and pathological aging have been extensively
54 investigated and specified (see Livingstone et al., 2020, for a recent review), a mechanistic
55 understanding of the neural bases underlying individual differences with advancing age remains
56 to be further developed. Achieving this goal requires the use of highly sensitive methods, and
57 the investigation on brain activity with high spatial and temporal resolutions.

58 The concept of cognitive reserve has originally been proposed to improve our
59 understanding of mechanisms underlying sustained cognitive performance in spite of age-
60 related and pathology-related brain changes (Stern, 2002). Over the last two decades, this
61 concept has undergone several changes and developments (see Cabeza et al., 2018; Stern et al.,
62 2020; Pascual-Leone & Bartrés-Faz, 2021). The current concepts of maintenance, resistance,
63 and resilience have been proposed to specify the heterogeneity brain and cognitive changes in
64 face of aging and neurodegenerative disease. During healthy aging, **maintenance** (Nyberg et
65 al., 2012) refers to the relative absence of brain changes with advancing age, while **reserve**
66 (Stern, 2002) encompasses the compensatory processes allowing the preservation of cognitive
67 performance in presence of structural and functional brain changes. The concept of reserve
68 involves two complementary aspects: brain reserve (i.e. individual differences in brain size,
69 number of synapses, etc.) and cognitive reserve (i.e. individual differences in the cognitive
70 processes and brain networks recruited to perform a given task). With the progression of
71 neurodegenerative disorders, **resistance** (Arenaza-Urquijo & Vemuri, 2018) defines the
72 protection of brain reserve against alterations and the prevention of brain lesions and damages
73 before their occurrence. Finally, **resilience** (Pascual-Leone & Bartrés-Faz, 2021) concerns the
74 processes involved in the compensation of changes occurring with the development of
75 neurodegenerative disorders, explaining various degrees of symptomatology in the face of an
76 equal pathological load. Some degree of overlap may exist between these concepts. As an
77 example, compensatory adjustments (e.g., increased frontal recruitment) might be implemented
78 in presence of both age- and pathology-related changes, yet qualitative differences may also be
79 observed between the adjustments implemented in response of healthy aging and pathology. A
80 recent review of Pascual-Leone and Bartrés-Faz (2021) specified these concepts and
81 emphasized the need for individually-based markers that could predict an individual's risk for
82 disability and cognitive decline.

83 Neuroimaging studies have been central in the emergence and evolution of the concepts
84 of reserve, maintenance, and resilience. Several decades of work aimed at investigating
85 structural (i.e., grey matter, white matter) and functional (i.e., local activity, association between
86 the activity of distinct brain regions) changes with age and pathology (e.g., Damoiseaux, 2017;
87 Spreng & Turner, 2019). Recent work revealed that these dimensions are closely related, with
88 large-scale brain functional network relying on a structural architecture of white matter fibers
89 (e.g., Hinault et al., 2019; Suárez et al., 2020). Indeed, preserved brain integrity has been
90 associated with preserved cognitive functioning. This work also identified compensatory
91 adjustments in older adults (i.e., larger activations, bilateral recruitment) associated with similar

92 cognitive performance to that of younger individuals (e.g., Cabeza et al., 2018). These studies
93 mainly relied on high spatial resolution methods such as functional magnetic resonance imaging
94 (fMRI), characterized by excellent spatial accuracy but low temporal resolution (in the order of
95 seconds). Therefore, the temporal dynamics of brain networks and the influence of age and
96 pathology on these dynamics remain poorly known. Investigating these dynamics with high
97 temporal-resolution methods (in the order of milliseconds) such as magnetoencephalography
98 (MEG) or electroencephalography (EEG) is important because higher cognitive functions such
99 as memory and cognitive control that are most affected by age and pathology involve multiple
100 cognitive processes in rapid successions and short durations (e.g., Courtney & Hinault, 2021).
101 Even when compensation may mask these changes in clinical or neuropsychological
102 assessment, specifying dynamic network connectivity may reveal alterations of the stability of
103 communications between brain regions, or delays in the fast succession of connectivity patterns,
104 providing a better understanding of concepts of reserve, maintenance, resilience and resistance.

105 The brain generates its own temporal structure, that is critical to the ways in which
106 signals are routed, combined and coordinated (e.g., Bao et al., 2015; Voytek & Knight, 2015).
107 Brain rhythms present the particularity of being observed across species (e.g., Buzaki 2006),
108 which suggest a major evolutionary advantage of rhythmic communications (e.g., Miller et al.,
109 2018). Brain rhythms are distinguished in different frequency bands (delta (1-4Hz), theta (4-
110 8Hz), alpha (8-12Hz), beta (12-30Hz), gamma (30-45Hz)). Magnetoencephalography and
111 electroencephalography (M/EEG) methods enable the investigation of these rhythms and
112 dynamic connectivity patterns in humans (e.g., Baillet et al., 2017). Given the critical
113 involvement of coordinated brain rhythms in higher-order cognitive processing, age-related
114 changes in the dynamic of brain communications may act as a marker for cognitive decline in
115 older adults. Such complex interplay across rhythms is highly sensitive to structural changes
116 and the progression of neurodegenerative disorders (e.g., Courtney & Hinault, 2021; Gaubert
117 et al., 2019), as even small changes of dynamic synchrony can lead to cognitive decline with
118 aging (e.g., Hinault et al., 2020, 2021; Kumral et al., 2021).

119 Here, we review EEG and MEG studies in healthy older individuals and in patients to
120 identify elements that shed new lights on cognitive aging and pathology effects. We focus on
121 three main patterns: 1) compensatory or resilience adjustments when brain dynamics are
122 altered, 2) maintenance of these dynamics in the face of aging or pathology and 3) non-effective
123 or maladaptive changes related to normal aging or pathology. These concepts have been
124 extensively investigated with fMRI, we thus aimed at highlighting the complementary
125 contribution of M/EEG findings. M/EEG can indeed detect between group differences in the
126 initiation, maintenance, or interruption of brain communication at the sub-second level, which
127 is therefore highly sensitive to early disruptions associated with age and pathology. In this
128 review, we will first present studies contributing to these concepts in healthy aging before
129 presenting work on pathological aging. Given the work conducted in pathological aging, we
130 focused on Alzheimer's disease and his preclinical stage the Mild Cognitive Impairment (MCI).
131 We conclude with recommendations and future directions that could guide and stimulate future
132 studies. Such endeavor could lead to new cognitive stimulations strategies targeting brain
133 rhythms, and reduce the cognitive decline commonly associated with age.

134

135 **1. Normal aging**

136 Nineteen M/EEG studies including younger (20 years - 30 years) and older (60 years - 85
137 years) healthy participants have been selected, investigating cognitive performance and neural
138 synchrony data (see table 1). We will describe here three of the most commonly used

139 techniques. First, the Phase locking value (PLV; Lachaux et al., 1999) measures whether the
140 oscillatory phase of the activity of a group of neurons, in a certain frequency band, can
141 transiently synchronize with those of another group of neurons. This transient phase-locking
142 has been associated with communications between neural groups (Fries et al., 2015). A second
143 technique similar to this is the Phase lag index (PLI; Stam et al., 2007), which measures the
144 asymmetry of the distribution of phase differences between two signals. Finally, coherence
145 (Nunez et al., 1997) measures the associated of signals' amplitudes across brain regions. These
146 measures and provides information about neural synchrony and the presence of functional
147 connectivity between brain regions. The main results studied in this section are illustrated in
148 Figure 1.A.

149 **1.1. Compensation**

150 In older individuals with similar levels of cognitive performance as younger individuals,
151 previous MRI studies have shown that older individuals frequently engage additional brain
152 regions, as described in the CRUNCH (Compensation Related Utilization of Neural Circuit
153 Hypothesis. Reuter-Lorenz & Cappell, 2008) model. This increased recruitment of brain
154 regions has been associated with cognitive performance, and is referred to as compensation
155 (Cabeza et al., 2018). Angel et al. (2010, 2011) investigated this phenomenon in EEG using
156 ERP (Event-related potential). They revealed larger bilateral activity in older individuals with
157 higher cognitive performance. M/EEG studies critically identified that an increased
158 synchronization of fronto-parietal regions has been observed in older individuals showing
159 preservation of cognitive functioning. Ariza et al. (2015) asked healthy young and elderly
160 participants to perform an interference-based working memory task in which participants were
161 asked to memorize a face/sound pair (a face was displayed and associated with a semantic
162 attribute). The pair was followed by an interference phase during which a known face with a
163 question about that person was presented to them. Finally, a recognition phase in which
164 participants were asked to tell whether the presented pairs were the same as those presented in
165 the encoding phase. This study reported a global increase in alpha synchrony (measured by
166 PLV) in older individuals compared to younger individuals, while both groups showed similar
167 cognitive performance. This increased alpha synchrony has only been observed during the
168 interference period, and has been interpreted as a compensatory mechanism in older individuals.

169 Using an inhibitory task, Hong et al. (2016) showed that an increase in phase synchrony of
170 the delta and theta frequency bands localized at the fronto-central and parieto-central areas
171 reflected a compensatory phenomenon in healthy older individuals (see also Phillips &
172 Takeda, 2010, for similar findings in the gamma frequency band). Also, a posterior-anterior
173 synchrony switch (increase of delta synchrony in anterior versus posterior position) was also
174 found to be compensatory for a face emotion recognition task (Aktürk et al., 2020). These
175 compensatory phenomena are not only found in cognitive tasks, but also for motor tasks. Rosjat
176 et al. (2021), for example, showed increases in delta and theta synchrony (measured by PLV)
177 in healthy elderly, in association with sustained motor performance at the same level as in young
178 people (see also Rosjat et al., 2018).

179 **1.2. Maintenance**

180 Increased brain activity is not systematic and it is important to note that some individuals
181 do not need to implement these compensations, possibly because of higher cognitive reserve
182 levels (Stern et al., 2009). Lopez et al. (2014b), in a study comparing the global connectivity
183 (with PLV and PLI) of older participants with higher or lower cognitive reserve, showed
184 compensatory phenomena from the latter group only. Indeed, while cognitive performance was
185 similar between low and high reserve participants, individuals with lower reserve showed

186 increased in theta, alpha and beta synchrony in frontal, temporal and occipital regions. This
187 suggests that some individuals show a more efficient network functioning and therefore do not
188 need to engage a more extended brain network. Relatedly, Ho et al. (2012) showed that lower
189 theta and alpha synchrony levels (measured with coherence and phase-locking measures) in the
190 parietal region, associated with similar performance than younger individuals.

191 Maintenance thus refers to the preservation of similar brain activity levels than younger
192 individuals, allowing cognitive abilities to be relatively preserved with advancing age (Nyberg
193 et al., 2012). MRI work showed, for example, that older individuals with little changes in
194 functional activity during encoding, relative to younger adults, can sometime perform better
195 than older individuals with larger activation changes (Duzel et al., 2011). Studies on this
196 phenomenon are, to our knowledge, rare. Rondina et al. (2019) investigated the preservation of
197 brain dynamics with aging, using a spatial memory task where participants were asked to
198 remember the spatial location of three objects seen separately. In the test phase, participants
199 were then asked to determine whether the location of the objects was the same or different than
200 in the memory phase. They revealed that older individuals showed a similar pattern of brain
201 activations than young participants, with an increase theta band oscillatory activity in occipital
202 regions, and a decrease in frontotemporal regions. The maintenance of this brain activity pattern
203 was associated with similar cognitive performance between age groups. Also, in a visual
204 attention task, young and older individuals showed a similar pattern of increased lower gamma
205 frequency activity in the frontal region with increasing task difficulty (Phillips & Takeda,
206 2010). Moreover, Coquelet et al. (2017) investigated MEG phase synchrony at rest and reported
207 a maintenance of the electrophysiological connectome with age. Coquelet and colleagues
208 observed similar patterns between age groups in the alpha and beta frequency bands. The
209 maintenance of synchrony in the beta band was positively correlated with the maintenance of
210 cognitive performance in older individuals.

211 This functional maintenance seems to critically depend on the maintenance of the
212 underlying structures of the brain networks. Hinault et al. (2020) investigated the structure-
213 function relationship between Diffusion Tensor Imaging (DTI) and EEG data of neuronal
214 synchrony (PLV) of young and old healthy participants. Authors used an arithmetic task, in
215 which participants had to maintain, or update, arithmetic operations (addition, multiplication)
216 in working memory in order to determine whether proposed equation results (e.g., $8 \times 4 = 36$)
217 were correct or incorrect. Preserved integrity of white matter fibers at a similar level to younger
218 participants, in some older individuals, was associated with preserved functional synchrony in
219 the alpha and gamma frequency bands, and similar cognitive performances between age groups.
220 In particular, the inferior fronto-occipital tract was associated to functional coupling between
221 the inferior frontal gyrus and the occipital lobe. These results also illustrate the strong
222 association with the preservation of brain reserve, which would enable such maintenance (Stern
223 et al., 2009).

224 Thus, the maintenance of functional synchrony with age (at rest and during task completion)
225 is associated with the preservation of cognitive functions in healthy elderly individuals. This
226 maintenance has mainly been observed between frontal and parietal regions. However, the
227 preservation of this functional synchrony at a similar level to younger individuals is frequently
228 associated with an increased synchrony in other brain regions. Liu et al (2017) showed that a
229 maintenance of delta and theta synchrony of central regions (measured with the PLI), in the
230 absence of increased activity in other regions, was associated with decreased motor and
231 cognitive performance. This suggests that maintenance is strongly linked to the presence of
232 functional compensations. However, such increased brain activity could also be deleterious,
233 reflecting network alteration and the presence of excitotoxic or neurodegenerative phenomena
234 (Hillary & Grafman, 2017).

235 **1.3. Non-effective changes**

236 With advancing age, changes in brain function can be compensatory (as discussed above),
237 but may also turn out to be ineffective. In an EEG study (Toth et al., 2014), young and old
238 healthy participants had to perform a working memory task consisting of remembering coloured
239 squares at certain locations. During the test phase, these squares remained at the same locations
240 but could change in colour. Participants had to determine whether squares were identical to
241 those displayed during the encoding phase or not. Synchrony was determined with the PLI
242 measure, and a specific decrease in theta synchrony between frontal and posterior sites was
243 observed in healthy older adults compared to younger individuals (see also Li & Zhao, 2015).
244 Importantly, this theta synchrony decrease has been associated with lower cognitive
245 performance. Also, increased high gamma synchrony in the left frontal region during a maze
246 task (visual planning task) has been shown to be negatively associated with performance (Paul
247 et al., 2005).

248 In one of our studies (Jauny et al., 2022), we showed that maladaptive changes can be
249 identified in resting-state activity. This study involved the Cam-CAN cohort (e.g., Shafto et al.,
250 2014; Taylor et al., 2017) and changes in synchrony (with the PLV measure) as well as directed
251 connectivity (with the entropy transfer measure, which provides a directed connectivity
252 measure) were investigated. We observed a greater variability in brain networks' synchrony
253 over time relative to younger individuals, mainly for the Default Mode Network (DMN; this
254 network is mainly activated when no task is proposed from the participant and plays a role in
255 continuous environmental monitoring; Uddin et al., 2019) in the delta frequency band.
256 Moreover, we showed that older individuals showed a reversed dominant direction in
257 information transfer, relative to younger individuals, with a significant increase in the anterior
258 to posterior direction of functional connectivity. These changes were correlated with a decline
259 in cognitive performance on tests measuring working memory, attention and logical reasoning
260 (also Sahoo et al., 2020). This reversal of the dominant information transfer direction could
261 represent a failed compensation attempt. The increases in brain synchrony studied could also
262 reflect excitotoxic processes (Hillary & Grafman, 2017; Mai & Howell, 2019), with increased
263 activity preceding neuronal loss. Indeed, older individuals showing these hyperconnectivity
264 phenomena had decreased cognitive performance.

265 As we have seen in these different sections, changes in synchrony vary over time and with
266 task difficulty, and increased synchrony is not always beneficial. These changes appear to be
267 related to changes in the level of white matter fibers integrity (Hinault et al., 2020, 2021).
268 Indeed, with the presence of white matter lesions has been associated with decreased brain
269 synchrony (Wessel et al., 2016). In association with the influence of potentially preclinical
270 excitotoxic processes, structural and functional changes could reflect the progression of
271 neurodegenerative disorders.

272 **2. Pathological Aging**

273 In this part, we considered M/EEG study involving patients with Alzheimer's disease (AD)
274 and its prodromal stage called MCI (Mild Cognitive Impairment). AD is the most common age-
275 related pathology and is characterized by memory and cognitive control impairment (involving
276 inhibition, planification and mental flexibility; Baudic et al., 2006). The investigation of early
277 AD stages such as the MCI stage is of significant interest because some individuals will later
278 develop AD while others will remain stable or develop other pathologies such as, for example,
279 frontotemporal or vascular dementia (e.g. Perez-Gonzalez et al., 2014; Jongsiriyanyong &
280 Limpawattana, 2018). The reviewed studies were selected based on the same criteria as in the

281 previous section on normal aging (see table 1). The main results studied in this section are
282 illustrated in Figure 1.B.

283 **2.1. Resilience**

284 In line with the reserve concept developed in healthy older individuals, resilience refers to
285 the processes involved in coping with the development of neurodegenerative disorders and the
286 associated brain changes (Pascual-Leone & Bartréz-Faz, 2021). Indeed, resilience allows, like
287 reserve, the preservation of cognitive functions in spite of brain changes. Few studies have
288 documented this phenomenon. Gaubert et al. (2019) compared resting state EEG data (phase
289 synchrony calculated using PLV and PLI) from preclinical AD patients (at two AD progression
290 stages), and control participants. They observed that the degree of neurodegeneration (measured
291 by the level of amyloid beta load) impacted functional connectivity. Higher alpha functional
292 connectivity in parieto-occipital sites was observed when amyloid load levels were low. This
293 increase in alpha connectivity was interpreted as reflecting a compensatory phenomenon, as
294 patients showed normal cognitive performance (measured by the Free and Cued Selective
295 Reminding Test, assessing episodic memory). In presence of high amyloid loads, theta
296 functional connectivity was decreased. It was suggested that amyloid deposits could negatively
297 impact the extracellular environment, preventing compensatory adjustments. Moreover, Bajo
298 et al. (2010) administered a memory task to healthy elderly MCI participants with similar
299 performance levels than controls. They reported an increased interhemispheric gamma, beta,
300 and alpha synchrony in MCI participants compared to controls. This increase in synchrony has
301 been interpreted as reflecting compensatory adjustments in MCI individuals. The presence of
302 interhemispheric activity is in line with the HAROLD (Hemispheric Asymmetry Reduction in
303 Older; Cabeza, 2002) model. Finally, an overall increase in theta synchrony has been reported
304 in fronto-occipital and right parieto-temporal areas for MCI individuals during the performance
305 of a mental arithmetic task thus allowing the maintenance of cognitive performance (Lopez et
306 al., 2014a).

307 These resilience phenomena have been reported in patients with MCI, but may not always
308 be necessary. Indeed, Lopez et al., (2014b) showed that increases in synchrony were reduced
309 in individuals with greater reserve.

310 **2.2. Resistance**

311 Resistance refers to the prevention of brain injury and damage before their occurrence
312 (Pascual-Leone & Bartréz-Faz, 2021). AD is characterized by advanced brain and cognitive
313 impairments, being the results of years of neurodegenerative processes, and therefore resistance
314 phenomenon can no longer be observed. However, investigating the earlier stages of this
315 disease, Lopez et al. (2014a) used a mental arithmetic task (mental subtraction) at two levels of
316 difficulty (subtracting from one to one, being the easy level, and subtracting from three to three
317 being the hard level). Both MCI patients and controls showed similar cognitive performance.
318 Furthermore, lower synchrony at rest, and increased delta synchrony in frontal interhemispheric
319 regions during task completion (measured with PLV), were similar across groups. Thus, there
320 seems to be a maintenance of certain brain functions in early AD stages. However, such
321 maintenance of specific brain communications was associated with compensatory increases in
322 synchrony in other brain regions in MCI patients. The concept of resistance, alone, would
323 therefore not allow the maintenance of cognitive performance in individuals at risk of
324 developing a neurodegenerative disease. Furthermore, increased synchrony in individuals with
325 MCI was initially associated with preservation of brain and cognitive functioning, but may also
326 be a sign of disease progression (Knyazeva et al., 2013).

327 **2.3. Maladaptive changes**

328 Despite the presence of maintained synchrony patterns and the ability of some individuals
329 to compensate for disease-related brain damage, individuals with MCI also exhibit brain
330 changes associated with impaired cognitive performance. For example, Caravaglios et al,
331 (2016) showed that increases in beta synchrony in aMCI patients correlated with poorer
332 performance on various neuropsychological tests (Trail making test, Rey Auditory Verbal
333 Learning Test, Semantic Verbal Fluency). Maladaptive changes thus occur and could be due to
334 disturbances in the integrity of white matter fibers. Altered white matter integrity has indeed
335 been shown to result in decreased alpha synchrony in individuals with MCI, particularly in
336 parietal regions (Teipel et al., 2009). Synchrony analyses have also revealed decreased
337 connectivity in frontal and parieto-temporal alpha and beta activity, especially in
338 interhemispheric couplings, associated with impaired cognitive performance (digit verbal span
339 task; Li et al., 2019).

340 Thus, maladaptive changes appear to differ depending on AD progression level. Garn et al,
341 (2015) revealed that qEEG markers such as decreased delta synchrony in parietal regions could
342 have a predictive role in AD severity. Indeed, synchrony measures could discriminate between
343 SCD (Subjective Cognitive Decline; defined by a subjective complaint without cognitive
344 impairment), MCI, and AD individuals (Houmani et al., 2018). Using measures of synchrony
345 (bump model) and complexity (epoch-based entropy), the authors discriminated AD patients
346 from SCD patients with high specificity (91.6% accuracy, 100% specificity and 87.8%
347 sensitivity). Their results showed that AD patients showed increased EEG synchrony in the
348 theta band on frontal and occipital region compared to SCD patients. These differences could
349 be explained by the degradation or lower cognitive reserve in AD patients (Montemurro et al.,
350 2021).

351

352 **Discussion**

353 Results reviewed here highlight the importance of considering the temporal dynamics
354 of brain activity, and synchronized brain communications, to our understanding of cognitive
355 reserve, resilience and maintenance in healthy and pathological aging. Dynamic connectivity
356 patterns must display both stability and flexibility as a function of the cognitive process
357 involved, and task context. While the stability of dynamics in the network engaged is important
358 to process relevant information, flexibility is required to adjust to goal changes and to inhibit
359 the processing of irrelevant information (e.g., Voytek & Knight, 2015). Cognitive decline
360 during healthy and pathological aging can result from impairments of such dynamic network
361 activity. While further investigations remain necessary, the present review summarizes current
362 work on the association of sustained, increased or altered neural synchrony across brain regions,
363 with cognitive preservation or decline.

364 While reserve has been associated with increased frontal synchrony in the theta and
365 alpha bands (Ariza et al., 2015; Hong et al., 2016), resilience has been associated with increased
366 alpha, beta and gamma synchrony (e.g., Bajo et al. 2010). It is important to note that not all
367 changes are associated with a relative preservation of cognitive performance. Indeed,
368 maladaptive changes have also been reported, such as the increased delta synchrony in posterior
369 regions (Jauny et al., 2022). Findings suggest that (a) the neural mechanisms involved in both
370 reserve and resilience could be partly similar, and (b) resilience could involve a stronger
371 involvement of higher frequency bands relative to reserve. This difference could be determined
372 by the degree of preservation of the structural network integrity, which is modulated by the
373 pathology progression, leading to different compensation levels. Yet, whether differences

374 across reserve and resilience are mainly of quantitative nature, or also qualitative, remains to
375 be further clarified.

376 Maintenance-related patterns were also observed in healthy older individuals, with a
377 relative absence of impairments in fronto-parietal communication dynamics associated with
378 preserved cognitive performance (Hinault et al., 2020, 2021, Rondina et al., 2019). The brain's
379 structure-function interplay appears to be at the heart of the heterogeneity associated with
380 maintenance during aging (Courtney & Hinault, 2021; Jauny et al., 2022). Indeed, maintenance
381 was observed with preserved dynamics in the relative absence of integrity loss. Conversely,
382 reserve-related adjustments are a necessity in presence of reduced structural integrity. The
383 inability of any of these two mechanisms will lead to cognitive decline. Additional longitudinal
384 studies remain necessary to further specific the concepts of maintenance and resistance
385 mechanisms. Another open question for future research lies in the distinction between
386 hyperactivation or hyperconnectivity resulting from (a) failed compensatory attempts, although
387 that some degree of network reorganization has been implemented, and (b) excitotoxic
388 processes associated with the progression of neurodegenerative disorders. Direct investigations,
389 associated with longitudinal follow-up, will be necessary to further clarify this distinction.

390 While these findings are promising, they only reflect a fraction of M/EEG aging studies.
391 Future studies in the field could integrate the following recommendations to further address the
392 contribution of brain dynamics. First, while resting-state measurements are indicators of the
393 potential for brain networks' reorganization in cognitively challenging situations, they cannot
394 always inform on their actual implementation and association with specific cognitive processes.
395 Although few studies were conducted to address these issues, we expect that dynamic stability
396 and flexibility of task-related networks could provide critical elements regarding subsequent
397 cognitive changes and the effect of cognitive stimulation programs. In line with recent
398 questioning in the field (e.g., Finn, 2021), it also appears critical to question whether resting-
399 state recording can precisely measure elements of cognitive reserve. Although changes can be
400 observed in brain activity at rest, specific task-related delays in the implementation,
401 maintenance or interruption of communications across brain regions could be highly sensitive
402 to age and pathology effects. Recent work (Babiloni et al., 2020; Guntenkin et al., 2021)
403 highlighted the clinical value of investigating oddball-related brain activity to detect pathology
404 effects. Finally, from an epidemiological perspective, future studies should also consider
405 middle-aged individuals (40-60 years) to clarify the association between changes in brain
406 dynamics and later cognitive trajectories. Indeed, age-related brain changes occur throughout
407 life, and changes in older individuals (> 65 years) may be the result of earlier brain changes.
408 Also, it appears critical that future studies include a more diverse population, especially in terms
409 of education level (de Olivera et al., 2018; Ashby-Mitchell et al., 2020). Indeed, most of the
410 reviewed studies considered populations with a high level of education, which limits the
411 investigation of reserve and resilience mechanisms.

412 Many studies relied on methods that are blind to temporal changes, such as amplitude
413 comparison following averaging of large time periods. This facilitates data analyses but could
414 lead to missing important information. Hidden-Markov models (Tibon et al., 2021) or
415 multiscale entropy (McIntosh et al., 2014) enable the specification of time-varying connectivity
416 states, which could further our understanding of the heterogeneity of cognitive aging. Finally,
417 the majority of the reviewed studies involved sensor-based analyses and brain connectivity
418 methods, such as coherence analyses. While the reviewed work reveals important patterns
419 associated with resilience and maintenance, they are prone to volume conduction effects (e.g.,
420 Brunner et al., 2016) and suffer from low spatial accuracy. A more generalized use of non-
421 biased connectivity estimates (e.g., Allouch et al., 2020), associated with source reconstruction
422 of M/EEG activity, could clarify some open questions and replicate the currently reported

423 findings. This would also enable the investigation of the same networks and regions of interest
424 as previous fMRI work (Pascual-Leone & Bartres-Faz, 2021), to specify their time course and
425 dynamics.

426 Brain connectivity changes observed in M/EEG could differentiate individuals
427 according to pathology stages (Houmani et al., 2018) in a non-invasive manner. These data
428 could also help predicting pathology progression. Specifying rhythmic brain communication
429 changes with age and pathology could also guide direct modulations of brain rhythms through
430 targeted stimulations. Recent work, such as Reinhart et al. (2019), revealed the feasibility of
431 short-term interventions using tACS (transcranial Alternative Current Stimulation; application
432 of a low intensity current to the brain with electrodes in order to synchronize or desynchronize
433 brain oscillations) on working memory performance in healthy older adults. Improved working
434 memory performance (up to 50 min post-stimulation) has been reported in healthy older adults
435 following frontotemporal theta stimulation relative to a sham condition. Several points, such as
436 the long-term benefits of these interventions, together with the optimal number of sessions,
437 remain to be specified. Such knowledge could lead to new specific and neurophysiologically
438 grounded intervention targeting disrupted brain communications and enhancing rhythms
439 associated with successful compensation, suggesting an intense development of this research
440 field in the coming years.

441 **Author Contributions Statement**

442 GJ: Investigation, Writing; FE: Supervision, Review; TH: Conceptualization, Supervision,
443 Writing, Review.

444 **Conflict of Interest Statement**

445 The authors report no declarations of interest.

446

447 **References**

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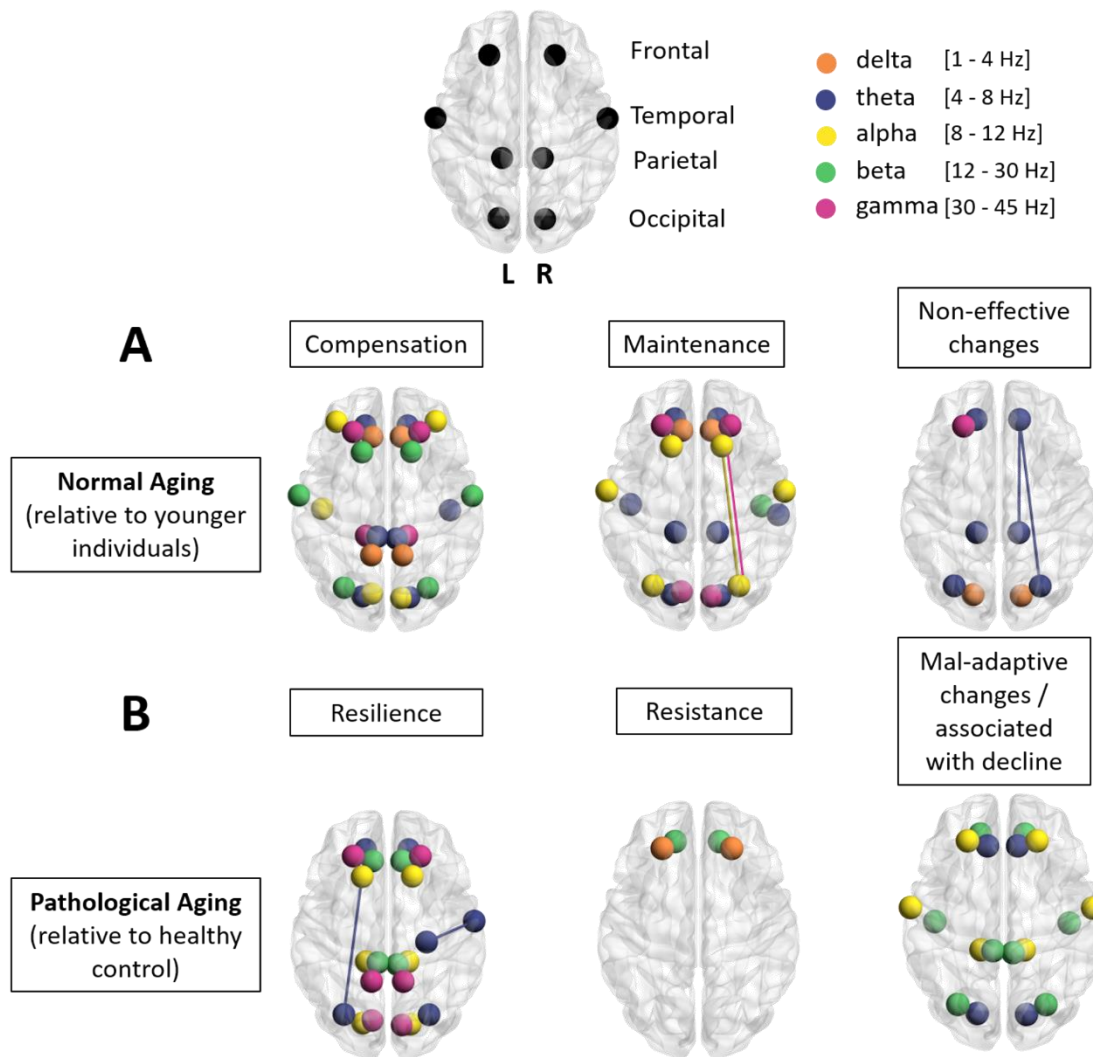
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717 **Figure 1:** Illustration of the main results of this study: Each point represents a brain region
 718 and each color a frequency band (orange: delta; blue: theta; yellow: alpha; green: beta, pink:
 719 gamma). (A): Normal Aging. This row of three brains summarizes the main results found in
 720 this review (change in synchrony in different regions for different frequency bands relative to
 721 younger individuals) for the notions of compensation, maintenance and non-effective changes
 722 in normal aging. (B): Pathological Aging. This row of three brains summarizes the main results
 723 found in this review (change in synchrony in different regions for different frequency bands,
 724 relative to healthy controls) for the notions of resilience, resistance and maladaptive changes
 725 in pathological aging. Using BrainNet-viewer tool.

726 **Table 1:** *Summary table of the results*

Healthy Aging							
Lead author	Publication date	Measure	Method	Task	Participants (age)	N	Results
Compensation							
Ariza et al.	2015	MEG	PLI	Working memory	Young healthy adults (21.88) Older healthy adults (64.45)	9 11	The global increase in alpha synchrony is positively correlated with the maintenance of cognitive performance in the elderly group
Aktürk et al.	2020	EEG	Coherence	Facial expressions recognition task	Young healthy adults (24) Older healthy adults (62.07)	15 15	Increased delta, theta, and alpha synchrony in frontal position in healthy elderly would allow maintenance of cognitive performance compared to the young
Hong et al.	2016	EEG	Phase synchronization analysis	Go/NoGo	Young healthy adults (21.4) Older healthy adults (61)	23 18	Increased delta and theta phase synchronization in the fronto-central and parieto-central areas is associated with the maintenance of cognitive performance for the elderly group
Phillips & Takeda	2010	EEG	PLV	Visual search	Older healthy adults (68)	14	Increased gamma synchronization in the fronto-parietal position is positively correlated with cognitive performance in the elderly group
Rosjat et al.	2018	EEG	PLV	Finger tap	Young healthy adults (22-35) Older healthy adults (60-78)	21 31	Maintenance of the increase in delta synchronization in the elderly (similar to the young group) could enable the maintenance of cognitive performance in this same group compared to the young group

Rosjat et al.	2021	EEG	PLV	Finger tap	Young healthy adults (22-35) Older healthy adults (60-78)	21 31	Maintenance of the increase in delta and theta synchronization in the elderly (similar to that of the younger group) would allow the maintenance of cognitive performance
Maintenance							
Coquelet et al.	2017	MEG	Power envelope correlation	Resting state	Young healthy adults (23.6) Older healthy adults (68.8)	25 25	Maintenance of synchrony in beta band in elderly at a similar level than the young group is positively correlated with cognitive performance
Hinault et al.	2020	EEG	PLV	Working memory	Young healthy adults (23.2) Older healthy adults (71.0)	40 40	Older with preserved integrity of white matters fibers show preserved functional synchrony in alpha and gamma band and no difference in cognitive performance with younger participants
Ho et al.	2012	EEG	Phase locking measures and coherence	Attention task	Young healthy adults (23.7) Older healthy adults (70.1)	15 15	Decreased theta and alpha synchronization in the parietal region are positively correlated with cognitive performance in the elderly group (No difference in cognitive performance between groups)
Liu et al.	2017	EEG	PLI	Finger tap	Young healthy adults (22-35) Older healthy adults (60-78)	18 24	Maintenance of delta and theta synchronization of central regions in the elderly group associated with poorer cognitive performance compared to the young group

Lopez et al.	2014(b)	MEG	PLV and PLI	Sternberg task	Older healthy adults high cognitive reserve (67.3) Older healthy adults low cognitive reserve (69.7)	9 12	The low reserve group shows an increase in theta (fronto-parietooccipital), alpha (fronto-temporo-occipital) and beta (parieto-fronto-temporo-occipital) connectivity would allow maintenance of cognitive performance compared to the high reserve group
Rondina et al.	2019	MEG	Phase synchronization analysis	Spatial memory	Young healthy adults (24.8) Older healthy adults (65.9)	16 16	Increased theta synchrony in occipital regions and decreased theta synchrony in fronto-temporo-parietal regions in the elderly in a manner similar to the young group allows maintenance of cognitive performance for the older group
Non-effective changes							
Hinault et al.	2021	M/EEG	PLV	Working memory	Young healthy adults (23) Older healthy adults (71)	40 40	Decreased structural integrity in the elderly group alters the stability of communications (alpha and gamma frequency bands) between brain regions compared to the young group
Jauny et al.	2022	MEG	PLV and TE	Resting state	Young healthy adults (26.5) Older healthy adults (64.5)	46 46	Increased variability of delta synchrony in the DMN network and reversal of information transfer in the anterior to posterior direction of functional connectivity with age correlates with decreased cognitive performance
Li & Zhao	2015	EEG	PLV	Visual search	Young healthy adults	13	Increased theta and alpha centro-frontal synchrony and decreased beta centro-

					(23.9) Older healthy adults (63.1)	13	parietal synchrony in the older group could explain the decreased cognitive performance compared to the younger group
Paul et al.	2005	EEG	Phase synchrony	Maze test	Young healthy adults (24.6) Older healthy adults (58)	160 100	Increased gamma2 synchrony in left frontal areas correlated with decreased cognitive performance for the older group
Sahoo et al.	2020	MEG	Coherence	Resting state	Young healthy adults (18-35) Older healthy adults (66-88)	126 216	The decrease in alpha synchrony correlates with the decrease in cognitive performance on the VSTM test
Toth et al.	2014	EEG	PLI	Working memory	Young healthy adults (21.1) Older healthy adults (65.8)	20 16	Decreased theta synchronization between frontal and posterior regions could explain the decreased cognitive performance in the older group
Wessel et al.	2016	EEG	PLV	Cognitive control	Older healthy adults (62) Older adults with focal frontostriatal lesion of white matter (62.42)	12 12	The lesion group shows a decrease of beta synchrony
Pathological Aging							
Lead author	Publication date	Measure	Method	Task	Participants (age)	N	Results

Resilience							
Bajo et al.	2010	MEG	Synchronization Likelihood	Memory task	Older healthy adults (71.6) MCI patients (74.8)	19 22	Increased alpha, beta and gamma synchronization in MCI participants is associated to the preservation of cognitive performance compared to the healthy elderly group
Gaubert et al.	2019	EEG	PLV	Resting state	Older healthy adults (75.62) preclinical AD patients (76.88)	175 25	Increased alpha synchrony in preclinical ADs with low amyloid levels would allow preserve of cognitive performance at a level similar to healthy elderly. Amyloid deposits could have a negative impact on the extracellular environment, preventing compensatory adjustments.
Lopez et al.	2014(a)	MEG	PLV	Resting state and working memory	Older healthy adults (71.8) MCI patients (72.5)	32 38	An overall increase in theta synchrony was reported in the right fronto-occipital and parieto-temporal regions for the MCI group, as well as an increase in delta synchrony in the interhemispheric frontal regions. All this would allow the MCI group to have similar cognitive performance to the healthy elderly group
Resistance							
Knyazeva et al.	2013	EEG	S estimator	Resting state	Older healthy adults (67.6) AD patients (68.7)	15 15	Increased synchrony in individuals with MCI was initially associated with preservation of brain and cognitive functioning, but may also be a sign of disease progression
Lopez et al.	2014(a)	MEG	PLV	Resting state and working memory	Older healthy adults (71.8) MCI patients (72.5)	32 38	An overall increase in theta synchrony was reported in the right fronto-occipital and parieto-temporal regions for the MCI group, as well as an increase in delta synchrony in the interhemispheric frontal

							regions. All this would allow the MCI group to have similar cognitive performance to the healthy elderly group
Maladaptive changes							
Caravaglios et al.	2016	EEG	coherence	Resting state and omitted tone task	Older healthy adults (69.6) aMCI patients (68.1)	15 15	Increase in beta synchrony in aMCI patients correlated with poorer performance on various neuropsychological tests
Garn et al.	2015	qEEG	Coherence	Resting state	AD patients (76) probable AD patients (75)	118 79	qEEG synchrony markers could predict AD severity
Houmani et al.	2018	EEG	Bump model	Resting state	SCD participants (68.9) AD patients (81.6)	22 49	Discrimination of SCD and AD groups based on synchrony measures
Li et al.	2019	EEG	PLI	Digit verbal span task	Older healthy adults (62.75) mild AD patients (72.5)	8 6	The decrease of connectivity in the alpha and beta frequency bands in frontal and parieto-temporal areas is correlated with impaired cognitive performance
Teipel et al.	2009	EEG	Coherence	Resting state	Older healthy adults (67.0) aMCI patients (73.6)	20 16	The decrease of white matter integrity causes a decrease in alpha synchrony for aMCI participants

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728 *EEG: Electroencephalography; MEG: Magnetoencephalography; PLI: Phase Lag Index; PLV: Phase Locking Value; TE: Transfer Entropy*