Brain-printing biometrics underlying mechanism as an early diagnostic technique for Alzheimer’s disease neurodegenerative type

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1. Introduction

Alzheimer’s disease (AD) is a progressive neurodegenerative disease that results in a loss of neuronal viability within the cortex and hippocampus as well as other brain regions important for cognition. A main goal for slowing disease progression lies in identifying individuals in the early asymptomatic stage, several years before the appearance of the neuropsychological hallmarks of AD (Van Deerlin, 2012; Holzer et al., 2013). Such specific high-quality early detection techniques can provide patients with the time needed to make life plans regarding their careers or other personal issues, in addition to identifying plans to help manage their treatment. Even for familial forms of AD, especially the rare form known as early-onset familial Alzheimer disease (eFAD) that is associated with mutations in genes encoding the amyloid precursor protein (APP), presenilin-1, and/or presenilin-2, it would be valuable to have a diagnostic technique that predicts the onset of the disease (Haupt et al., 1992; Nochlin et al., 1993; Campion et al., 1999). Nowadays, novel biometric techniques have been widely explored as “Hidden Signature Biometrics.” The goal of these commonly used biometric devices such as sMRI (Aloui et al., 2011; Naït-ali et al., 2020) or EEG (Palaniappan, 2008; Naït-ali 2020) is to extract a large number of features from inaccessible areas of the human body for the purpose of authorized personal identification.

Meanwhile examining changes in brain structure and electrical signals that accompany the onset of AD using the brain printing biometrics technique (BPB) would allow neurologists to determine whether BPB can serve as a reliable, noninvasive technique for early AD diagnosis. The onset of AD typically correlates with the overexpression of Aβ in brain tissue (Bae and Yi, 2020; Calabrò et al., 2021). At this early stage, the profound structural changes that occur can be correlated with the BPB technique which would be designed to generate personalized IDs using both computerized brain structural analysis as well as brain activity via sMRI (Chen et al., 2014) and EEG intra-connected devices, respectively (Jackson and Snyder, 2008). The current review highlights the idea that AD can be characterized and diagnosed by monitoring the early morphological and structural changes developed during the preclinical stage using the BPB technique. The use of this proposed approach would provide early and accurate AD diagnosis before the deposition or appearance of irreversible AD hallmarks in different brain areas. Additionally, the BPB technique would provide insight into the sequences of pathogenic events that occur in AD in addition to previously characterized preclinical inflammatory features and events associated with the sequences.
1.1. Proposed brain-printing biometrics technique

Biometrics were recently developed as an authorized digital form of storage for unique human measurable characteristics from various areas of the body with the goal of achieving nearly 100% accurate identification of individuals. The technique takes advantage of unique, inherited, characteristics as personal identifiers. Several types of biometrics are well-known, including physiological shape biometrics, behaviorometrics, and, finally, hidden structure biometrics, the latter represented in the current review as brain-printing biometrics (Aloui, Nait-ali and Naceur, 2012; Barra et al., 2017). The idea of using the BPB approach in the early identification of significant cognitive disease modifications, including hallmark AD depositions, is mainly based on the fact that in addition to the early influence of neuroinflammation and genetic mutations on brain structural morphology, altered brain features have been linked to, and used in the detection of, long term brain disorders (Nochlin et al., 1993; Campion et al., 1999; Aloui et al., 2011). Diagnosing Alzheimer’s disease was and still is mainly based on identifying the neuropathological hallmarks in the patient’s brain, a positive family history, and/or genetic screening for familial forms of AD, all of which can be described as late-stage methods of AD diagnosis. The amyloid cascade hypothesis assumes that different inherited congenital defects or other unknown inflammatory and environmental factors may lead to direct or indirect over-accumulation of toxic Aβ, resulting in severe brain tissue damage many years before disease diagnosis. This highlights the importance of developing a reliable, noninvasive early method of detecting AD (Jackson and Snyder, 2008; Barra et al., 2017; Calabro et al., 2021).

The BPB approach described here is proposed to be a precise, noninvasive technique for early diagnosis that utilizes two forms of computerized, interconnected mapping techniques: sMRI (Fujita and Hagiwara, 2019) and EEG (Tsolaki et al., 2014) for detecting unique structural and electrical alterations, respectively (Fig. 1). sMRI is used for deep brain image scanning to identify the onset of brain deformities

![Brain Biometrics System Diagram](image-url)
and associated unique hidden brain structural changes before or as the
disease precipitates, including the surface area of brain, white/gray
matter volume, cortical-subcortical folds, and brain gyrification index
(Aloui et al., 2012; Chen et al., 2014; Fujita and Hagiwara, 2019)
(Fig. 1). EEG, on the other hand, measures brain function at different
frequencies and can report the degree of deterioration (Jackson and
Snyder, 2008; Tsolaki et al., 2014) (Fig. 1).

1.2. Alzheimer’s disease and brain-printing biometrics technique

Despite the dramatic increase in the prevalence rate, AD has been
severely underdiagnosed, misdiagnosed, or the diagnosis delayed until
later stages when treatments are no longer beneficial and oligomeric
aggregation hallmarks are irreversible (Relkin, 2000). Apart from
misdiagnosis, the eFAD inherited form is mainly identified by a positive
family history and the AD inflammatory form by hallmark Aβ aggrega-
tions that give rise to brain atrophy. Although the family history maybe
80% negative, the probability of having the eFAD gene mutation re-
mains high, as the negative family history instead may be due to the
early death or misdiagnosis of affected family members (Kaye, 1998;
Relkin, 2000). Furthermore, AD inflammatory forms can also be mis-
diagnosed because of the dependence on the appearance of hallmarks of
AD in different brain regions that usually appear at a late stage already
associated with the symptoms of irreversible cognitive dysfunction. The
inclusion of very late misdiagnosed patients in BPB studies may there-
fore lead to serious consequences, including the appearance of extreme
mental, behavioral and functional disabilities associated with structural
deformities that occur within a short time frame as well as vague pre-
disposing factors that produce biased outcomes and incorrect feedback.
For these reasons, careful consideration must be given to creation of the
inclusion and exclusion criteria. On the other hand, raising awareness
about identifying AD forms at an early asymptomatic stage might give
neuroscientists the chance to find novel agents and palliative treatments
that could delay or block severe disease progression (Braak and Braak,
1997; Kaye, 1998). The BPB technique allows us to hypothesize that AD
can be accurately noninvasively distinguished from other neurodegen-
erative diseases, including inheritance and other high risk inflammatory
forms of AD, by generating a characterized diagnostic feature to be
named as “AD-BPB early hidden structural modifications.”

Fig. 2. Proposed BPB imaging modifications detection and verification technique.
1.3. Brain-printing biometrics technique implementation

The new approach of measuring BPB for early AD detection is based on designing the brain biometrics computerized intervention system (BBCIS) (Fig. 1), which will be conducted on suspected AD patients with early cognitive signs. The construction of BBCIS includes eight phases as follows: the 1st and 2nd phases depend on creating a secret key and ID for the purpose of authentication/identification of each enrolled patient, followed by the acquisition of brain images performed by sMRI (phases 1 and 2) (Figs. 1 and 2). The 3rd phase includes the acquisition of EEG brain wave signals and their integration with simultaneous sMRI imaging (Figs. 2 and 3). The next two phases (4 and 5) include respective brain image slicing, segmentation, and analysis of extracted features (volume, surface and boundaries) (Fig. 4). While the 7th phase includes creating computerized artificial brain transformation and coordination analysis and then storing the data/geographical changes under the previously identified secret ID key assigned to each enrolled patient for the eight assessed phases (Figs. 2–4). Concerning the last phase, which mainly depends on raw data imaging and the analysis of brain waves, the degree of association depends on using preprocessing, extraction, and sequencing tools along with the appropriate use of ROC curve to avoid high image false-positive results (Fig. 4). In contrast, routine sMRI and EEG will be conducted weekly on the suspected AD subjects at certain fixed time intervals in order to detect morphological brain changes from one week to another.

1.4. Cortical thickness and brain-printing biometrics

It was previously reported that AD is highly associated with detected changes in the cortical thickness, especially in the frontal, temporal and occipital lobes (Lerch et al., 2005). The early decrease in cortical thickening as a drawback of AD is highly consistent with the BPB theory. Cortical thickness analysis via BPB allows searching for the direct link between cortical depth and clinical or psychological variable conditions across the entire brain surface (Lerch et al., 2005; Du et al., 2007). Brain-printing biometrics share many advantages over other global search algorithms, including voxel-based morphometry (VBM) and complicated deformation field analysis. Unlike VBM, a definite accurate description of the cortical thickness in millimeters allows promising quantitative descriptive results enabling successful early disease detection (Lerch et al., 2005; Du et al., 2007). Since significant disadvantages of using cortical thickness via MRI include failure to detect subcortical structures and white matter areas (Du et al., 2007; Querbes et al., 2009), measuring the cortical thickness deformities via BPB provides vast advantages for measuring WM and subcortical structures changes with high accuracy. Additionally, it directly links cortical thickness and the degree of cognitive impairment in AD (Lerch et al., 2005; Lerch and Evans, 2005).

1.5. Effect of psychological and physiological factors on BPB

BPB is suggested to be affected by different psychological and physiological factors such as vascular diseases, stress, anxiety, and sleep disorders (Marsland et al., 2015). Thus, these factors have to be excluded to avoid results bias (Curie et al., 2013; Marsland et al., 2015). Other factors such as medications may cause a power increase in both beta and theta bands resulting in results falsification (Blume, 2006). Emotional states may also induce different functional connectivity...
patterns in brain waves (Chan et al., 2015). It was also found that patients suffering from AD exhibit lower EEG, especially in the theta band, than normal controls (Lerch et al., 2005; Radić et al., 2019). Thus, developing a stable and efficient BPB system requires understanding its features in order to maintain high accuracy. AD-related inflammatory markers are associated with total brain volume changes (TBV) and primary brain structural morphology (Marsland et al., 2015). It was reported that increased neuroinflammation would result in increased white matter hyperintensities (WMH) and decreased TCB. These recognized changes can be used as an early diagnosis parameter for AD prior to the appearance of hallmark depositions (Jefferson et al., 2007). YKL-40, known as chitinase 3-like 1 protein, has been identified as the primary marker of glial inflammation and was found to be significantly higher in AD patients than in other types of neurodegenerative diseases. Some studies also reported variations in the YKL-40 level during predementia stages, where YKL-40 has also been reported to be higher in the cerebrospinal fluid (CSF) of AD patients indicating the progressed neurodegenerative pathophysiological process in brain tissues (Alcolea et al., 2015) (Table-1). Furthermore, patients with high sensitivity C-reactive protein (hsCRP) showed a decrease in cortical gray matter volume (Taki et al., 2013) (Table-1). Additionally, elevated levels of plasminogen activator inhibitor-1 (PAI-1) can also be correlated with low speed and motor coordination, in addition to a significant loss in WM regions in cortico-subcortical regions. The cortical thickness was also found to be attenuated with elevated IL-6 level indicating general cortical atrophy (McCarrey et al., 2014) (Table-1). These observed changes can be considered a consequence of the onset of AD-associated progressive damage (Miralbell et al., 2012; Anwar et al., 2021a, b) (Table-1).

Meanwhile, high serum TNF-α level was found to be associated with alterations in the gray matter GM structural network volume (Taishi et al., 2007; Benson et al., 2020).
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