OPEN ACCESS
International Journal of Neural Systems, Vol. 34, No. 2 (2024) 2350069 (16 pages)

DOI: 10.1142/S0129065723500697

Discriminative Power of Handwriting and Drawing Features in Depression

Claudia Greco*, Gennaro Raimo†, Terry Amorese‡ and Marialucia Cuciniello§
Department of Psychology, Università della Campania "Luigi Vanvitelli"
Viale Ellittico 31 Caserta 81000, Italy
**claudia.greco@unicampania.it*
†*gennaro.raimo@unicampania.it*
‡*terry.amorese@unicampania.it*
§*marialucia.cuciniello@unicampania.it*

Gavin Mcconvey
Action Mental Health, 27 Jubilee Rd, BT23 4YH
Newtownards, UK
gmcconvey@amh.org.uk

Gennaro Cordasco¶
Department of Psychology, Università della Campania "Luigi Vanvitelli"
Viale Ellittico 31 Caserta, 81000, Italy
gennaro.cordasco@unicampania.it

Marcos Faundez-Zanuy
Tecnocampus Universitat Pompeu Fabra
Carrer d'Ernest Lluch 32 Mataro, Barcelona 08302, Spain
faundez@tecnocampus.cat

Alessandro Vinciarelli
University of Glasgow, School of Computing Science
18 Lilybank Gardens Glasgow, G12,8RZ, Scotland
alessandro.vinciarelli@glasgow.ac.uk

Zoraida Callejas-Carrion
Department of Languages and Computer Systems, Universidad de Granada
Periodista Daniel Saucedo Aranda Granada, 18071, Spain
zoraida@ugr.es

Anna Esposito
Department of Psychology, Università della Campania "Luigi Vanvitelli"
Viale Ellittico 31 Caserta, 81000, Italy
anna.esposito@unicampania.it

Received 1 April 2023
Accepted 3 November 2023
Published Online 24 November 2023

¶Corresponding author.

This study contributes knowledge on the detection of depression through handwriting/drawing features, to identify quantitative and noninvasive indicators of the disorder for implementing algorithms for its automatic detection. For this purpose, an original *online* approach was adopted to provide a dynamic evaluation of handwriting/drawing performance of healthy participants with no history of any psychiatric disorders ($n = 28$), and patients with a clinical diagnosis of depression ($n = 27$). Both groups were asked to complete seven tasks requiring either the writing or drawing on a paper while five handwriting/drawing features' categories (i.e. pressure on the paper, time, ductus, space among characters, and pen inclination) were recorded by using a digitalized tablet. The collected records were statistically analyzed. Results showed that, except for pressure, all the considered features, successfully discriminate between depressed and nondepressed subjects. In addition, it was observed that depression affects different writing/drawing functionalities. These findings suggest the adoption of writing/drawing tasks in the clinical practice as tools to support the current depression detection methods. This would have important repercussions on reducing the diagnostic times and treatment formulation.

Keywords: Depression; handwriting; on-line analysis; behavioral signs; mental health.

1. Introduction

Depression is considered one of the most important challenges in mental health and the major cause of disability worldwide.[1] Globally, more than 300 million people suffer from this psychiatric disorder and recently, due to the COVID-19 pandemic, these numbers have dramatically increased.[2] Depression significantly burdens work or school life, sleeping and eating habits and physical health.[3] Besides, the cognitive and behavioral impairments associated with this disorder also produce social disabilities, such as isolation or avoidance of affective relationships which in turn, lead to a life quality's pauperization.[4]

Depression disorder's symptomatology include depressed mood, anhedonia, weight and sleep disorders, psychomotor disturbances (retardation or agitation), fatigue, decreased ability to focus, feeling of worthlessness or extreme guilt and suicidal thoughts. According to the DSM-V, the diagnosis of depression requires five or more symptoms, including at least either the depressed mood or anhedonia, to be present within a 2-week period.[5] However, due to the very heterogeneous nature of depression, a successful diagnosis and the subsequent effective treatment could be difficult to formulate in the clinical practice. In addition to this, depression usually overlaps with other disorders or syndromes, which decreases the likelihood to make a proper diagnosis, especially at the early stages.[6]

A major reason behind the incorrect or late diagnoses is the absence of accepted objective criteria for the assessment of depression, and more in general for any other psychiatric disorder.[7] Indeed, currently the diagnosis of depression is carried out only through clinical interviews and self-reported questionnaires. However, unbiased information for supporting the diagnosis could be obtained by the analysis of objective behavioral signals such as speech, physiological data, text analysis, or handwriting.[8–17] These measures could serve as impartial criteria to favor the detection of depression at early stages and prevent the worsening of the symptoms, which in turn would lighten the burden of the disease also in terms of costs and public care.[18]

Among these indicators, handwriting could represent a quantitative index of psychomotor symptoms of depression.[19] Psychomotor disturbances can include slowed thought processes, physical restlessness or severe retardation in gross and fine body movements.

Current neurobiological models of depression suggest that the altered psychomotor functioning is associated with frontostriatal abnormalities such as white matter changes in the basal ganglia and decreased volumes of the prefrontal cortex, caudate, and putamen. Also, the altered initiation and progression of motor activity in depression have been associated with impairments in activation of the motivational and cognitive control systems, due to dysfunctions in the dopaminergic and serotonergic neurotransmission.[19–21]

Regardless of the still debated exact neural basis of psychomotor disturbances in depression, these symptoms are considered a central feature of the disorder and source of rich clinical information. Indeed, it has been suggested that they have high discriminative validity and may be the sole symptoms that can discriminate between depression subtypes and are predictive of positive outcome to the medical treatments.[21–24] Therefore, it would be relevant for the clinical practice to identify measurable features that are able to detect the psychomotor changes occurring with depression.

To this regard, the handwriting could be particularly useful since it is a unique and complex human activity requiring the synchrony of motor, cognitive, perceptual, and affective components.[25] Due to the various processes involved, its assessment has proved to be very informative about personality traits,[26] emotional states,[27] neurodegenerative pathology,[28] and mental health issues.[29]

Moreover, in recent years, handwriting data have been examined through machine-learning (ML) and deep-learning (DL) techniques to exploit their clinical discriminative potential in the development of computer-aided diagnosis systems. Literature on the topic revealed that measurements extracted from handwriting patterns can successfully classify control and clinical groups.[30–33]

Considering these results, it has been hypothesized that the analysis of handwriting's features such as pressure, velocity, space occupied with the traits, number of traits or inclination, could be effective in detecting depressive states and discriminating between individuals suffering from depression and healthy subjects. However, few studies have investigated the relationship between depression and handwriting changes. To this regard, the following section provides a brief literature review on the topic.

1.1. *Handwriting and depression: State of the-art*

The first studies on the subject examined the differences in the handwriting related to time features between healthy and depressed patients.[34–36] By using a digitalized tablet and a special pen, participants were required to engage in some drawing tasks with different complexity (e.g. simple lines, letters, familiar and nonfamiliar figures, etc.). Results of these studies unanimously pointed out that depressed patients were significantly slower than healthy ones both in starting the first drawing movement and completing the tasks, by supporting the hypothesis that timing handwriting features were able to detect psychomotor retardation symptoms and discriminate between groups.

Such results were also found in Ref. 37 which compared kinematic features of velocity, amplitude, and regularity between healthy controls and depressed patients and found that the latter were slower in completing handwriting tasks (e.g. drawing circles, writing a sentence). Reference 38 broadened the investigation by including, besides the temporal features, also those related to space and pressure. Their sample was composed of healthy and elderly participants suffering from mild depression who were required to copy a paragraph, fill out a check, write their own name, and write the alphabet in sequence. Results showed that the measures which most discriminated between the two group were the pressure's ones: Depressed patients applied significantly less pressure in all the four tasks, compared to healthy ones. In addition, compared to healthy controls, depressed patients showed greater slowness when they had to write their own name and reduced stroke width in the paragraph copying task. Likewise, Ref. 39 compared the kinematic measures in healthy controls and elderly participants diagnosed with mild major depressive disorder through the clock drawing test.[40] Compared to healthy participants, the clinical group reported significant lower strokes' height, width and length, while the number of strokes and temporal measures did not differ between groups. Other studies[41,42] have adopted a different approach based on the graphology analysis performed by forensic experts with the aim to identify features in the graphic content specific for depression (e.g. tremors in the writing, descending traits, irregularly sized letters, shape of letters). However, these studies reported no statistically significant differences between controls and patients with depression.

Concerning the studies examining the data-driven identification of depression, the literature reports that the handwriting features have not been sufficiently investigated in relation to this psychiatric condition (for a review, see Ref. 43). Indeed, in the existing handwriting datasets, depressive or negative emotional states have been assessed through self-reported measures.[27,44] To the best of our knowledge, there are no datasets which have collected handwriting recordings from individuals clinically diagnosed with a depressive disorder. Nevertheless, classification studies testing the discriminative power of handwriting data performed on such datasets report high accuracy results.[45–47]

As suggested by the results in the literature, handwriting features could be able to discriminate between depressed and nondepressed individuals. However, the above-mentioned studies present some limitations; for example, most of them focused only on elderly participants, whereas other studies did not consider participants' gender in the experimental design, or more in general, they adopted a graphological static approach based on the accordance degree among external observers, which takes into account only the geometry of the handwritten pattern, rather than a dynamic one which can also provide information about the underlying generation process. Nonetheless, the handwriting analysis seems to represent a promising methodology to detect depressive states and its investigation needs to be deepened in order to be included in the clinical practice and within research settings.

This research was conducted in the context of the "Mental health monitoring through interactive conversations" (MENHIR) Project. MENHIR is a H2020 Research and Innovation Staff Exchange project aiming to research and develop automatic systems devoted to promote mental health and assist people with mental ill health (depression and anxiety) to manage their conditions.

Following the "online" approach already adopted by the previous studies,[48,49] this paper presents a dynamic evaluation of depressed and nondepressed individuals' handwriting and drawing performance, by extending the investigation carried out in Ref. 17. This original approach to handwriting analysis has been possible due to the development of pencil and digital tablets, which enable to carry out the analysis of several parameters on computerized platforms with two major advantages. First, data collection includes nonvisible measurements such as the pressure applied on the paper, the pen inclination, in-air movements (i.e. pen movements at a small distance from the sheet of paper), which has been demonstrated to be as informative as the on-paper ones.[27,50] Second, the online approach allows to extract temporal information of the ongoing writing and drawing activities for each performed task, instead of obtaining just the single offline shot of the final outcome.

In the preliminary study,[17] the authors examined the writing and drawing skills among the following:

- Patients formally diagnosed with depression by a mental health-care expert (henceforth "Clinical group");
- Participants with no diagnosis of depression but who were categorized as "severe" or "extremely severe" in the depression sub-scale of the Depression Anxiety Stress Scales (DASS-21[51]; see the procedure section of this paper for a description of the tool). This group will be referred to as "DASS-Severe" group;
- Participants who were categorized as "normal" by the same questionnaire. This group will be referred to as "DASS-Normal" group.

Participants were asked to sit in front of a digitalized tablet with a white sheet of paper placed on the tablet and complete different writing and drawing tasks. The experimental protocol administered to the clinical group was different from that presented to the other two. Hence, statistical analyses were performed only on data extracted from the four tasks that the two protocols had in common:

(i) Drawing of two pentagons;
(ii) Drawing of a house;
(iii) Writing an Italian sentence in cursive letters;
(iv) Drawing of a clock with hours and clock hands.

Seventeen features were considered (see Sec. 3.2 of Ref. 17 for a list) and partitioned into five categories: Pressure, ductus, time, space, and inclination.

Several repeated measures ANOVAs were carried out to evaluate the efficacy of the considered features in differentiating the groups of participants. Results revealed some significant differences among groups. Concerning the ductus category, the clinical group was associated with higher number of traits (in-air, on-paper, and not recognized by the tablet) in all the fours tasks, compared to the other two groups. For the time category, results revealed that depressed patients were the slowest in drawing the two pentagons and writing the sentence in cursive letters, followed by the "DASS-Severe" group and the "DASS-Normal" group. Finally, the results showed that the clinical group significantly applied less pressure compared to the DASS-normal group in the two-pentagons and the house drawing tasks. No significant effects due to the depressive state were found in the space and inclination features' categories.

Starting from these promising findings, this research adopted the same "online" approach and procedure to further explore the discriminative power of the handwriting analysis in depression. The two studies share the goal of identifying which quantitative and objective features may enable discriminating between individuals suffering from depressive disorder and healthy ones. However, this work attempts to overcome some methodological limitations reported in the preliminary study and introduces new aspects:

- The investigation was broadened by recruiting a brand-new sample from a country different from Italy and Northern Ireland, so that the existing database of behavioral signs of depression would also include different cultural contexts.
- The numerosity within groups was increased to provide more robust statistical results.
- Gender of participants was counterbalanced in the sample in order to also test the role played by this variable.
- The experimental protocol was enriched both with more tasks and self-assessment measurements.
- A different statistical analysis model was applied to better fit the data.

2. Participants and Methods

Handwriting data were collected by using a WACOM INTUOS PRO series 4 digital tablet. The specifics of the tablet are as follows:

- Active area: (A5) 224 × 148 mm,
- Resolution: 5080 Lines per Inch (LPI).

To make the handwriting process as natural as possible, participants used an Intuos Inkpen (Pen pressure levels: 8192; Tilt recognition ±60 levels) which allowed them to visualize the strokes while they perform the tasks. In this way, it was possible to obtain information both on the strokes (through the sheet of paper), and on other parameters, as time information and in-air movements. Data were collected for several tasks and recorded in a comma separated values (CSV) file. The system registered the following data every 8 ms:

- The two-dimensional coordinates of the pen.
- The unix epoch (the number of milliseconds that have elapsed since 1, January 1970.
- The pen status: On paper = 1; in-air = 0 (when the pen is a few centimeters away from the paper); idle = not recorded but recognizable using timestamps.
- Two angles that describe the position of the pen with respect to the tablet.
- The amount of pressure applied by the pen on the paper, expressed using an integer value, from 0 (no pressure) to 8191 (maximum pressure).

In this study 17 features, related to five different categories (pressure, time, ductus, space, and inclination) have been considered for the analyses.

Figure 1 provides a description of the features. Note that the term "Stroke" indicates a maximal contiguous sequence of points belonging to the same pen status (on paper/in-air). These features have been selected both for testing in this context their effectiveness to discriminate between clinically depressed patients and healthy participants, and because they popped out from an automatic selection process exploiting a random-forest algorithm.[27] The following sections describe the sample characteristics and how they have been determined, the tasks used for data collection, the extracted handwriting features, and the description of the analyses.

2.1. *Participants*

Participants were recruited in different locations of Action Mental Health (AMH — https://www.amh.org.uk/), a nonprofit organization actively involved in the promotion of mental health and well-being of people in Northern Ireland.

To be included in the clinical group, the participants had to satisfy the following criteria:

- To be formally diagnosed of clinical depression by a mental health-care expert;
- To not be diagnosed with other psychiatric disorders (e.g. bipolar depression, schizophrenia) rather than anxiety because it is often associated with depression;

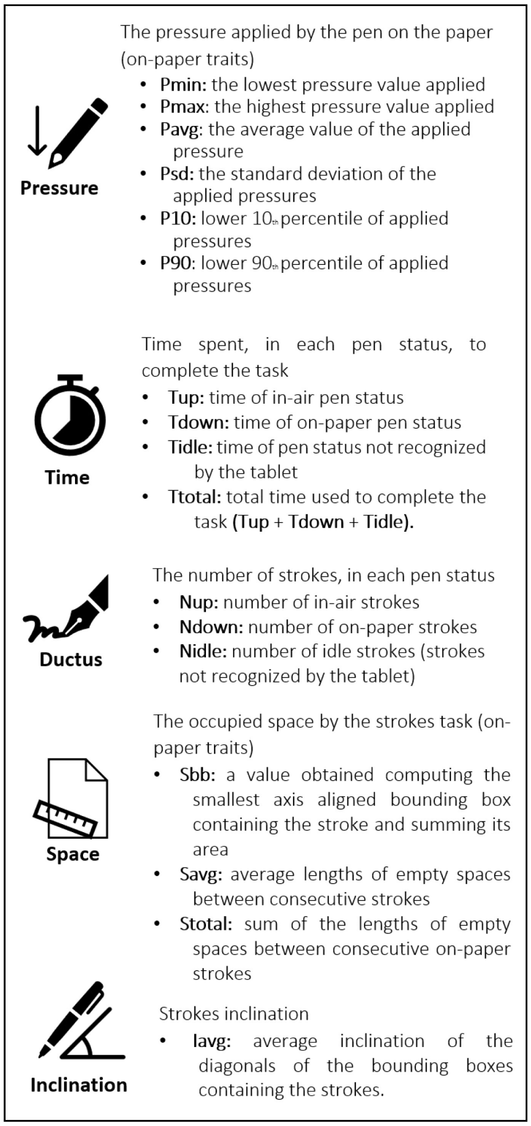

Fig. 1. Description of the features considered in the analyses.

- To obtain a score at the Beck Depression Inventory (BDI-II[52]) above the minimal range (≥ 14).

We decided to consider only the score of the BDI-II and not of the DASS-21 sub-scale of depression as inclusive criteria, since the former includes items covering the whole symptomatology of depression.

Inclusion criteria for the control group were no history or current conditions of no psychiatric disorders and a BDI-II's score within the minimal range (0–13).

The initial sample was composed of 66 participants (males = 32; mean age = 48.1; SD = 13). However, eight participants in the clinical group and six participants in the control one, were excluded from the analyses since they did not entirely fulfil the inclusion requirements. The final sample was composed of 55 participants (males = 28; mean age = 48.1; SD = 13). The clinical group consisted of 27 participants, and the control group consisted of 28 participants recruited among the AMH staff. Table 1 reports the demographic information and the sample distribution.

Table 1. Sample distribution with means (and s.d.) of participants' age and BDI-II score.

	Control group	Clinical group
Age	51.54 (12.7)	44.56 (12.7)
BDI-II	4.32 (0.81)	32.11 (1.93)
Gender		
Male	14	14
Female	14	13
Education		
Primary	1	2
Secondary	5	18
University	22	7

2.2. *Procedure*

Participants of both groups were required to follow the same procedure. The experimental setting consisted of a quiet room with enough space for a laptop and the digitalized tablet. Participants were invited to read the information sheet about the experiment, which described the research aims, type of data collected, risk and benefits of the participation, confidentiality and data treatment. After that, they were asked to sign the informed consent.

Experimental instructions required participants to sit in front of the digitalized tablet with a paper placed the tablet and complete seven different writing and drawing tasks. Figure 2 reports the A4 sheet with all the seven tasks and their execution order. The experimenter was located in front of the laptop while the participant carried out the experimental session, by saving each completed task as a separate CSV file through a dedicated handwriting capture software. Doing this, data could be analyzed separately for each one of them.

In detail, the instruction to complete each task requires to:

(i) Draw the two pentagons in the same configuration (example provided).

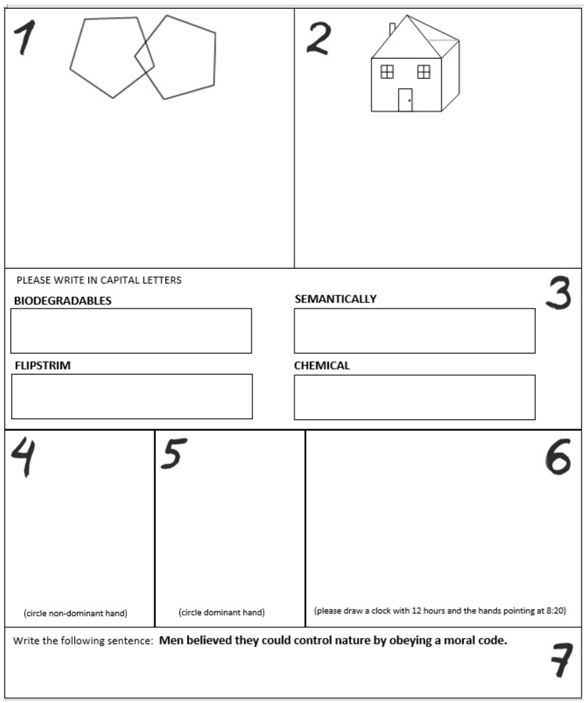

Fig. 2. Writing and drawing tasks performed by participants. Numbers indicate the execution order of the tasks.

(ii) Draw the house (example provided).
(iii) Write in capital letters the following four words: BIODEGRADABLES, FLIPSTRIM (a nonword), SEMANTICALLY, and CHEMICAL.
(iv) Draw a circle with the nondominant hand (no example provided).
(v) Draw a circle with the dominant hand (no example provided).
(vi) Draw a clock with 12 h and the hands pointing to 8:20 (no example provided).
(vii) Write in lowercase letters the sentence (i.e. a pangram): *Men believed they could control nature by obeying a moral code*.
(viii) After completing the handwriting tasks, participants were asked to complete two self-reported questionnaires in hard copy: The above mentioned BDI-II[52] and the DASS-21.[51] The BDI-II is composed by 21 group of statements, each one with four options, which measures the severity of depressive symptoms, by considering the last two weeks, from minimal range (none) to mild, moderate and severe. This questionnaire is based on the DSM-IV and follows its diagnostic criteria for depression.[5]

DASS-21 is also a self-assessment questionnaire estimating the level of depression, anxiety, and stress over the last week. Each scale consists of seven items, for a total of 21. Participants respond on a 4-point Likert scale (from 0: Did not apply to me at all; to 4: Applied to me very much or most of the time). Each subscale is associated with five severity labels: *normal*, *mild*, *moderate*, *severe*, *and extremely severe*. It should be noted that DASS-21 is not considered a clinical diagnostic measure, but it is frequently used in research to identify individuals with high distress who may experience depressive and anxiety states.

Questionnaires' scoring was subsequently elaborated and digitalized to be used for the analyses.

Once the self-assessment was concluded, participants were debriefed and thanked for their participation. The experimental session lasted approximately 15 min.

2.3. *Data analysis*

All the analyses were conducted with SPSS 21.0 IMB Software. The significance level was set at $p < 0.05$ and Bonferroni correction was applied in the main analyses (Multivariate analysis of variance, MANOVA) to the *p value* when multiple comparisons were carried out to assess differences among groups' means.

First, a U Mann–Whitney test was performed to test whether the depressed and control participants significantly differed from each other on the BDI-II and DASS scores and age.

In the second step, several MANOVAs were separately conducted for each category of measures to investigate whether the handwriting parameters were able to discriminate between depressed patients and nondepressed participants. Group (clinical versus control) and gender (male versus female) were inserted in the model as fixed factors, and the handwriting features were the dependent variables. For every handwriting category, seven different MANOVAs were separately conducted for each performed task. To avoid an overload of information, the following sections report only the significant effects that emerged from the analyses.

Table 2. Results of the U Mann-Whitney test on participants' age and means (and s.d.) of questionnaires' scores.

	Age	BDI-II	DASS-Depression	DASS-Anxiety	DASS-Stress	Total
Clinical Group	44.56	32.11	25.41	23.63	42.76	28
	(12.7)	(1.93)	(1.94)	(2.13)	(3.52)	
Control Group	51.54	4.32	2.36	2.29	5.64	27
	(12.7)	(0.81)	(0.64)	(0.76)	(0.82)	
Mann–Whitney U	267.500	3.500	16.500	6.000	0.000	
Z	−1.862	−6.375	−6.098	−6.257	−6.382	55
p	0.063	<0.001	<0.001	<0.001	<0.001	

3. Results

This section presents the results of the performed statistical analyses. MANOVAs' results are reported separately for each handwriting category.

3.1. *U-Mann–Whitney test*

Results revealed that the clinical group was associated with significantly higher scores in both questionnaires compared to the control group, whereas the age's mean was not significantly different (see Table 2 for statistical details).

3.2. *Pressure features*

No significant effect of the participants' group emerged in any of the tasks. A significant effect of gender was observed in the *nondominant hand circle drawing* task for the following features: Pmin ($F_{1,51} = 4.396$; $p = 0.041$; $\eta p^2 = 0.079$); Pmax ($F_{1,51} = 7.762$; $p = 0.007$; $\eta p^2 = 0.132$); Pavg ($F_{1,51} = 6.903$; $p = 0.011$; $\eta p^2 = 0.119$); Psd ($F_{1,51} = 6.820$; $p = 0.012$; $\eta p^2 = 0.118$); $P10$ ($F_{1,51} = 4.403$; $p = 0.041$; $\eta p^2 = 0.079$); $P90$ ($F_{1,51} = 8.067$; $p = 0.006$; $\eta p^2 = 0.137$).

More in detail, male participants (means: $P\text{min} = 540.82$; $P\text{max} = 16758.04$; $P\text{avg} = 13442.66$; $P\text{s.d.} = 2923.57$; $P10 = 10095$; $P90 = 16122.82$) were associated with higher values of all pressure features, compared to their female counterparts (means: $P\text{min} = 244.42$; $P\text{max} = 13654.90$; $P\text{avg} = 10585.47$; $P\text{sd} = 2505.14$; $P10 = 7566.91$; $P90 = 12914.29$).

3.3. *Time features*

Significant effects were found in the analyses concerning the following tasks (see Table 3 for means and S.D.):

- *Words writing*: there was a main effect of the group on tUp ($F_{1,51} = 18.928$; $p < 0.001$; $\eta p^2 = 0.271$); tDown ($F_{1,51} = 5.834$; $p = 0.019$; $\eta p^2 = 0.103$); tIdle ($F_{1,51} = 4.282$; $p = 0.044$; $\eta p^2 = 0.077$); Total ($F_{1,51} = 14.682$; $p < 0.000$; $\eta p^2 = 0.224$). Pairwise comparisons revealed that depressed patients spent more time both with the pen in-air and down on paper compared to healthy participants. Also, the time the pen was not recognized by the tablet was higher in the clinical group compared to the control one. Consequently, the total time used to

Table 3. Means (and s.d.) of time features as a function of group and task.

	tUp		tDown		tIdle		tTotal	
	Clinical group	Control group	Clinical group	Control group	Clinical group	Control group	Clinical group	Control group
Task								
Words	30044.44	18361.11	26794.28	20667.18	4486.35	2420.11	61326.08	41448.86
	(1916.73)	(1880.90)	(1810.60)	(1776.75)	(712.72)	(699.39)	(3702.63)	(3633.41)
Clock	26834.83	18350.75	17494.79	14442.96	11759.05	3889.21	56089.13	36682.93
	(2647.95)	(2598.46)	(1200.74)	(1178.29)	(3776.58)	(3705.98)	(5729.81)	(5622.71)
Sentence	19154.23	12082.39	20991.34	18721.32	2910.45	2067.43	43056.48	32872.07
	(1353.69)	(1328.38)	(1009.03)	(990.17)	(702.65)	(689.51)	(2318.86)	(2275.51)

complete the task was greater for depressed patients than healthy ones.

- *Clock drawing*: Participants' group exerted an effect on tUp ($F_{1,51} = 5.230$; $p = 0.026$; $\eta p^2 = 0.093$) and Total ($F_{1,51} = 5.844$; $p = 0.019$; $\eta p^2 = 0.103$). In detail, depressed patients were associated with greater time with the pen up in the air and time spent in completing the task compared to healthy participants.
- *Sentence writing*: Participants' group affected tUp ($F_{1,51} = 13.903$; $p < 0.001$; $\eta p^2 = 0.214$) and Total ($F_{1,51} = 9.827$; $p = 0.003$; $\eta p^2 = 0.162$). Also in this task, the clinical group spent more time in-air with the pen and to complete the task compared to the control one.

3.4. *Ductus features*

Results of the MANOVAs performed on the ductus features (see Table 4 for means and S.D.) were as follows:

- *House drawing*: A main effect of the group was observed on nUp ($F_{1,51} = 6.338$; $p = 0.015$; $\eta p^2 = 0.111$) and nDown ($F_{1,51} = 6.338$; $p = 0.015$; $\eta p^2 = 0.111$). Participants diagnosed with depression were associated with a lower number of pen strokes both in-air and on-paper, compared to healthy participants,
- *Words writing*: A main effect of the group was observed on nbIdle ($F_{1,51} = 8.351$; $p = 0.006$; $\eta p^2 = 0.141$), according to which the number of the pen strokes not recognized by the tablet was significantly higher in the clinical group (mean = 5.93) rather than in the control one (mean = 3.86),
- *Sentence writing*: A significant difference due to participants' group was observed on nUp ($F_{1,51} = 10.480$; $p = 0.002$; $\eta p^2 = 0.170$), nDown ($F_{1,51} = 10.480$; $p = 0.002$; $\eta p^2 = 0.170$) and nIdle ($F_{1,51} = 4.119$; $p = 0.048$; $\eta p^2 = 0.075$). Pairwise comparisons revealed that depressed patients made more strokes with the pen both in-air and on paper compared to healthy participants. Moreover, the number of not recognized strokes was greater in the clinical group than in the control one.

3.5. *Space and inclination features*

MANOVAs on spatial and inclination features showed the following results (see Table 5 for means and S.D.):

- *House drawing*: An effect of participants' gender was found on sAvg feature ($F_{1,51} = 5.507$; $p = 0.023$; $\eta p^2 = 0.097$), according to which the length of empty spaces between consecutive strokes (measured in pixels) was greater in female participants (mean:1849.41) compared to their male counterparts (mean:1605.94).
- *Circle with nondominant hand*: An effect of group was observed on Iavg feature ($F_{1,51} = 4.342$; $p = 0.042$; $\eta p^2 = 0.078$). Pairwise comparison revealed that depressed patients exhibited a more inclined trait compared to healthy participants when drawing the circle with the non-dominant hand (the greater the value, the less the inclination).
- *Clock drawing*: Participants' group affected the sBB feature ($F_{1,51} = 4.317$; $p = 0.043$; $\eta p^2 = 0.078$), according to which the clinical group the area occupied by the sum of the strokes (measured in square pixels) was smaller compared to control group.

Table 4. Means (and s.d.) of ductus features as a function of group and task.

	nUp		nDown		nIdle	
	Clinical Group	Control group	Clinical Group	Control group	Clinical Group	Control group
Task						
House	20.29 (1.15)	24.36 (1.13)	21.29 (1.15)	25.36 (1.13)	4.34 (0.91)	3.46 (0.89)
Words	67.14 (1.96)	64.36 (1.92)	68.14 (1.96)	65.36 (1.92)	5.93 (0.51)	3.86 (0.50)
Sentence	53.97 (2.64)	42.00 (2.59)	54.97 (2.64)	43.00 (2.59)	5.07 (0.76)	2.89 (0.75)

Table 5. Means (and s.d.) of space and inclination features as a function of group and task.

	sBB		sAvg		sTotal		Iavg	
	Clinical group	Control group	Clinical group	Control group	Clinical group	Control group	Clinical group	Control group
Task								
House	38593.20	38289.06	1747.14	1708.22	37637.43	43440.62	4.27	5.54
	(1887.27)	(1918.31)	(72.76)	(73.96)	(2463.86)	(2504.38)	(0.55)	(0.56)
Circle (Nondominant hand)	19889.19	19896.11	190.91	85.46	381.94	171.00	1.05	1.15
	(2170.56)	(2206.26)	(135.02)	(137.24)	(270.07)	(274.52)	(0.04)	(0.04)
Clock	72310.03	92754.55	1746.99	1989.47	45513.33	49951.16	3.06	3.11
	(6901.15)	(7014.65)	(146.07)	(148.47)	(4295.77)	(4366.42)	(0.22)	(0.23)
Sentence	108581.32	124034.55	1263.72	1801.72	65797.87	69627.78	1.65	1.59
	(5607.42)	(5699.64)	(111.52)	(113.36)	(3077.36)	(3127.97)	(0.18)	(0.18)

- *Sentence writing*: A main effect of the group was observed on the sAvg feature ($F_{1,51} = 11.447$; $p = 0.001$; $\eta p^2 = 0.183$): Depressed patients occupied less space than healthy ones during the sentence writing.

4. Discussion

Globally, more than 300 million people struggle with depression, a condition which severely affects the occupational, social and personal life, and at worse could lead to suicidal acts. Of all the individuals suffering from depression, only half of them get an effective treatment.[7] A major cause of so many untreated cases, lies in the difficulty to recognize this disorder, especially at early stages. The reason is that, according to the DSM criteria,[5] depression presents a very heterogeneous symptomatology with more than 1400 possible combinations of symptoms which can result in its diagnosis.[53] Moreover, depression usually emerges in comorbidity with other disorders or syndromes, increasing the diagnostic variety.

A possible solution to solve the diagnostic issues related to the depression would be including some objective criteria in its assessment, which currently relies only on clinical interviews and self-reported measurements.

Among the possible indicators, handwriting features have been considered as a quantitative index of depression, reflecting the psychomotor changes that characterize this condition. Not so many studies have investigated the handwriting patterns of depressed and nondepressed patients in order to test whether they can discriminate between the groups.[17,34–39] Nevertheless, findings reported in the literature support the hypothesis that the handwriting analysis could be useful in detecting depressive states.

In this context, this study intends to contribute knowledge on the discriminative power of handwriting features in detecting depression. Following the investigation of Ref. 17, this research adopted the same "online" approach providing a dynamic evaluation of the participants' handwriting and drawing performance.

Results of this work pointed out that handwriting features belong to all the considered categories, except pressure, successfully discriminate between depressed and non-depressed patients. To elaborate in detail, depressed patients seem to be slower than healthy controls in both drawing and writing tasks. This could be ascribed to a decreased processing speed which is closely linked to psychomotor retardation, and that leads to slower responses during tasks requiring attention and action planning.[54]

Concerning the ductus features, compared to healthy participants, depressed patients carried out the house drawing with less strokes, whereas they were associated with a greater number of strokes in the sentence writing task. This apparently inconsistent result may be explained by the type of task. Compared to the sentence writing, copying the drawing of the house probably required more attention to the details (e.g. the chimney, the knob of the door, the windows) and prolonged visuospatial abilities, which are two cognitive processes of psychomotor functioning that can be compromised in depression.[24] Supporting this hypothesis, a recent review[55] points out that depression could be associated with impairments in visual memory and executive functions, as planning actions to reach a specific goal.

The third and fourth handwriting features that were found to be different between depressed and non-depressed patients were those related to space and inclination of the trait. Both in a drawing task (i.e. clock drawing) and a writing one (i.e. sentence writing), depressed patients occupied less space on the paper compared to healthy participants by making smaller strokes. Moreover, patients exhibited a more inclined trait when they drew the circle with their nondominant hand. All these results could again be ascribed to the psychomotor disturbances of depression. Indeed, small and unsteady traits could reflect the less involvement of energy that people suffering from depression invest in their movements.[38,41]

Conversely to the findings of Ref. 17, in this work, pressure features did not differ between the groups, whereas significant results were found in the Northern Irish sample but not in the Italian one for what concerns the space and inclination features. Differences between the preliminary study and this one could be ascribed to different factors such as the different experimental protocol (even though some of the tasks were the same), the sample extracted from different population, or the different statistical model adopted.

Another possible factor which could account for the differences between the two studies was the educational background of participants: indeed, the literature claims a strong association between handwriting skills and educational achievement.[56,57] Therefore, writers of different countries, which are characterized by different educational learning systems, exhibit discriminative handwriting features.[58,59]

In this research, we did not consider the educational level in the main statistical model since the distribution of the education labels was not counterbalanced in the recruited sample, and the risk was to generate statistical comparisons characterized by too few cases. In this regard, future studies on the subject should definitely take into account this information to examine the role of education in the handwriting analysis.

Nevertheless, overlapping results among both studies were observed in the time and ductus categories, suggesting that temporal features and those related to the number of strokes could be effective in detecting clinical depressive states, regardless of the cultural context. However, in order to confirm such hypothesis, future studies should include cross-cultural comparisons to investigate the role of the cultural context in depressive symptoms' expression.

For what concerns gender differences, the current findings did not reflect the female prevalence of depression reported in the literature.[60] Indeed, no interaction effect between gender and group emerged for any features' category. However, it should be noted that, to the best of our knowledge, previous studies investigating handwriting and depression did not consider the participants' gender. Hence, it is not possible to establish whether the gender differences commonly associated with depressive disorders could be observed through handwriting analysis. Nonetheless, this study reported higher pressure applied in the nondominant hand circle task, and less space occupied while drawing the house by male participants compared to their female counterparts. These results are in line with the studies reporting gender differences in handwriting activity.[49,61]

Overall, this research attempts to address the diagnostic issues related to depression, and the obtained results represent a promising progress in the research field concerning the behavioral markers of this disorder. The rationale underlying this study is to highlight the need to identify unbiased evaluation criteria of this psychiatric condition that over the years has become a major challenge in mental health, by supporting the introduction of new assessment methods in the clinical practice.

Finally, this research does not suggest that handwriting changes could represent the sole markers for depression and does not claim a unique causal relationship between this psychiatric disorder and the above-mentioned measurements. However, the findings observed in this study corroborate the literature that have already demonstrated a relationship between psychomotor symptoms, which characterize depressive disorders, and the handwriting features.

To this regard, the current neurobiological models of depression suggest that alterations in psychomotor behavior are a significant aspect of the phenomenology of the disorder. As a result, they may represent a clinically relevant risk marker that could be assessed through a noninvasive methodology, such as the handwriting analysis.

5. Limitations and Future Directions

Besides the promising results, a main limitation of this study should be acknowledged. Due to privacy motives, it was not possible for the experimenter to get access to the clinical records of the patients before starting the recruitment. This means that the information about whether they were under medical treatment and the type of such medications was not reported, nor considered in the analysis. Of course, being on ongoing antidepressants would imply that some symptoms as psychomotor retardation (or agitation) could be mitigated by those treatments. However, the patients involved in the study were indicated by the mental-health experts as currently suffering from major depression, meaning that they were still experiencing symptoms related to the disorder. In addition, as a restorative measure to avoid that the lack of this information would affect the results, we included in the clinical group only those participants who outreached the minimal score in the BDI-II. This guaranteed that the depressive symptoms were present at the moment of the experiment's administration.

Another relevant limitation concerns the sample size. Due to this, the generalization of the obtained results should be made with caution.

To the best of our knowledge, the sample sizes of all the clinical studies involving handwriting data,[34–39,41,42] as well as those concerning the automatic detection of clinical conditions[30–33] are similar to the sample size reported in our study, given the difficulty to recruit this kind of patients. This occurs because engaging participants with these types of medical conditions may present several difficulties, due to their willingness and motivation to participate into any activities, especially nonfamiliar ones such as an experimental session.

Besides the limitations, this research has also some strengths. First, it contributes knowledge about the detection of depression through handwriting analysis with the aim to identify quantitative and noninvasive indicators of the disorder, which could be adopted in the clinical practice as a support tool to the current diagnostic methods. This would have important repercussions on the diagnostic times by preventing the worsening of the symptoms and, in turn, reducing the burden of the disease, both in terms of mental health and economic costs.

In addition, this paper presents a database of handwriting features which could be enriched with more data regarding the handwriting or other behavioral signs which could be altered in depression (e.g. speech, text, and facial expressions). Such extended database could serve to develop ML techniques, such as Support Vector Machines, Neural Networks or Bayesian Networks, equipped with the ability to pre-process, extract, and classify behavioral features belonging to different categories, by providing an accuracy score to increase the reliability and validity of the current experimental paradigm. A ML-based approach could generate new information from unstructured data, sourcing from different modalities, which can be useful for assisting mental health experts in the diagnosis and outcome prediction.[63–65] To support this, several studies successfully adopted ML and DL methods to detect the heterogeneous symptomatology of depression,[66,67] as well as other medical conditions, such as cognitive impairment,[68] Alzheimer's disease,[69] Parkinson's disease,[70] autism spectrum,[71,72] or epileptic seizure.[73,74]

Lastly, future directions may also consider to develop completely automated detection systems combining different types of data such as handwriting, drawing, speech, facial expressions, text content, electroencephalographic signals, by using ML or more complex DL methods, with the aim to include them in the clinical practice for the detection and assessment of depression.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author, [C.G.]. The data are not publicly available due to restrictions (they are containing information that could compromise the privacy of research participants).

Acknowledgments

This research leading to these results has received funding from the European Union Horizon 2020 research and innovation program under grant agreement No. 769872 (EMPATHIC) and No. 823907 (MENHIR), from the project SIROBOTICS that received funding from Ministero dell'Istruzione, dell'Università, e della Ricerca (MIUR), PNR 2015-2020, D.D. 1735/2017, from the project ANDROIDS that received funding from Università della Campania "Luigi Vanvitelli" inside the program V:ALERE 2019, funded with D.R. 906/2019, from the project SALICE that received funding from Università della Campania "Luigi Vanvitelli" inside the program Giovani Ricercatori (DR 509/2022), funded with DR 834/2022.

ORCID

Claudia Greco https://orcid.org/0000-0001-5871-4012
Gennaro Raimo https://orcid.org/0000-0002-8202-7711
Terry Amorese https://orcid.org/0000-0002-9987-2823
Marialucia Cuciniello https://orcid.org/0009-0003-3053-1881
Gennaro Cordasco https://orcid.org/0000-0001-9148-9769
Marcos Faundez-Zanuy https://orcid.org/0000-0003-0605-1282
Alessandro Vinciarelli https://orcid.org/0000-0002-9048-0524
Zoraida Callejas-Carrion https://orcid.org/0000-0001-8891-5237
Anna Esposito https://orcid.org/0000-0002-7268-1795

References

1. National Institute of Mental Health, Depression, *National Institute of Mental Health* (2022), https://www.nimh.nih.gov/health/topics/depression.
2. M. G. Mazza, M. Palladini, S. Poletti and F. Benedetti, Post-COVID-19 depressive symptoms: Epidemiology, pathophysiology, and pharmacological treatment, *CNS Drugs* **36**(7) (2022) 681–702.
3. U.S. Department of Health & Human Services, Does depression increase the risk for suicide?, *HHS. gov* (2015), https://www.hhs.gov/answers/mental-health-and-substance-abuse/does-depression-increase-risk-of-suicide/index.html.
4. F. Scibelli, A. Troncone, L. Likforman-Sulem, A. Vinciarelli and A. Esposito, How major depressive disorder affects the ability to decode multimodal dynamic emotional stimuli, *Front. ICT* **3** (2016).
5. American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 5th edn. (American Psychiatric Association, Arlington, VA, 2013).
6. S. Rodgers, M. Grosse Holtforth, M. Müller, M. P. Hengartner, W. Rössler and V. Ajdacic-Gross, Symptom-based subtypes of depression and their psychosocial correlates: A person-centered approach focusing on the influence of sex, *J. Affec. Disord.* **156** (2014) 92–103.
7. S. Mahato and S. Paul, Electroencephalogram (EEG) Signal Analysis for Diagnosis of Major Depressive Disorder (MDD): A Review, in *Nanoelectronics, Circuits and Communication Systems*, Lecture Notes in Electrical Engineering, Vol. 511 (Springer, Singapore, 2018), pp. 323–335.
8. M. Ahmadlou, H. Adeli and A. Adeli, Fractality analysis of frontal brain in major depressive disorder, *Int. J. Psychophysiol.* **85** (2012) 206–211.
9. M. Ahmadlou, H. Adeli and A. Adeli, Spatio-Temporal analysis of relative convergence (STARC) of EEGs reveals differences between brain dynamics of depressive women and men, *Clin. EEG Neurosci.* **44** (2013) 175–181.
10. U. R. Acharya, S. Vidya, H. Adeli, S. Jayashree, J. E. W. Koh and A. Adeli, Computer aided diagnosis of depression using EEG signals, *Eur. Neurol.* **73** (2015) 329–336.
11. U. R. Acharya, V. K. Sudarshan, H. Adeli, J. Santhosh, J. E. W. Koh, S. D. Puthankatti and A. Adeli, A novel depression diagnosis index using nonlinear features in EEG signals, *Eur. Neurol.* **74**(1–2) (2015b) 79–83.
12. U. R. Acharya, S. L. Oh, Y. Hagiwara, J. H. Tan, H. Adeli and D. P. Subha, Automated EEG-based screening of depression using deep convolutional neural network, *Comput. Methods Programs Biomed.* **161** (2018) 103–113.
13. J. Kim, Z. A. Uddin, Y. Lee, F. Nasri, H. Gill, M. Subramanieapillai, R. Lee, A. Udovica, L. Phan, L. Lui, M. Iacobucci, R. B. Mansur, J. D. Rosenblat and R. S. McIntyre, A systematic review of the validity of screening depression through Facebook, Twitter, Instagram, and Snapchat, *J. Affect. Disord.* **286** (2021) 360–369.
14. C. Greco, O. Matarazzo, G. Cordasco, A. Vinciarelli, Z. Callejas and A. Esposito, Discriminative power of EEG-based biomarkers in major depressive disorder: A systematic review, *IEEE Access* **9** (2021) 112850–112870.
15. L. Zhang, Y. Fan, J. Jiang, Y. Li and W. Zhang, Adolescent depression detection model based on

multimodal data of interview audio and text, *Int. J. Neural Syst.* **32**(11) (2022) 2250045.
16. S. Koops, S. G. Brederoo, J. N. de Boer, F. G. Nadema, A. E. Voppel and I. E. Sommer, Speech as a biomarker for depression, *CNS Neurol. Disord. Drug Targets* **22**(2) (2023) 152–160.
17. G. Raimo, B. Michele, M. Conson, G. Cordasco, M. Faundez-Zanuy, G. McConvey, S. Marrone, F. Marulli, A. Vinciarelli and A. Esposito, Handwriting and drawing for depression detection: A preliminary study, in *Proc. Int. Conf. AII 2022: Appl. Intell. Inf.*, eds. M. Mahmud, C. Ieracitano, M. S. Kaiser, N. Mammone and F. C. Morabito (Springer, Cham, 2022), pp. 320–332.
18. A. I. Turner, N. Smyth, S. J. Hall, S. J. Torres, M. Hussein, S. U. Jayasinghe, K. Ball and A. J. Clow, Psychological stress reactivity and future health and disease outcomes: A systematic review of prospective evidence, *Psychoneuroendocrinology* **114** (2020) 104599.
19. B. Liberg and C. Rahm, The functional anatomy of psychomotor disturbances in major depressive disorder, *Front. Psychiatry* **6** (2015) 34.
20. D. Chaudhury, H. Liu and M. H. Han, Neuronal correlates of depression, *Cell. Mol. Life Sci.* **72**(24) (2015) 4825–4848.
21. I. Grahek, A. Shenhav, S. Musslick, R. M. Krebs and E. H. W. Koster, Motivation and cognitive control in depression, *Neurosci. Biobehav. Rev.* **102** (2019) 371–381.
22. C. Sobin and H. A. Sackeim, Psychomotor symptoms of depression, *Am. J. Psychiatry* **154**(1) (1997) 4–17.
23. M. P. B. I. Pier, W. Hulstijn and B. G. C. Sabbe, No psychomotor slowing in fine motor tasks in dysthymia, *J. Affec. Disord.* **83**(2–3) (2004) 109–120.
24. D. Bennabi, P. Vandel, C. Papaxanthis, T. Pozzo and E. Haffen, Psychomotor retardation in depression: A systematic review of diagnostic, pathophysiologic, and therapeutic implications, *Biomed. Res. Int.* **2013** (2013) 1–18.
25. P. Werner, S. Rosenblum, G. Bar-On, J. Heinik and A. Korczyn, Handwriting process variables discriminating mild Alzheimer's disease and mild cognitive impairment, *J. Gerontol. B Psychol. Sci. Soc. Sci.* **61**(4) (2006) P228–P236.
26. A. Esposito, T. Amorese, M. Buonanno, M. Cuciniello, A. M. Esposito, M. Faundez-Zanuy, M. Likforman-Sulem, M. T. Riviello, A. Troncone and G. Cordasco, Handwriting and drawing features for detecting personality traits, in *Proc. 10th IEEE Int. Conf. Cognitive Infocommunications (CogInfoCom)* (IEEE, 2019), pp. 79–84.
27. L. Likforman-Sulem, A. Esposito, M. Faundez-Zanuy, S. Clemencon and G. Cordasco, EMOTHAW: A novel database for emotional state recognition from handwriting and drawing, *IEEE Trans. Hum. Mach. Syst.* **47**(2) (2017) 273–284.
28. C. Taleb, M. Khachab, C. Mokbel and L. Likforman-Sulem, Feature selection for an improved Parkinson's disease identification based on handwriting, in *Proc. 1st Int. Workshop on Arabic Script Analysis and Recognition (ASAR)* (IEEE, 2017), pp. 52–56.
29. P. Singh and H. Yadav, Influence of neurodegenerative diseases on handwriting, *Forensic Res. Criminol. Int. J.* **9**(3) (2021) 110–114.
30. J. Garre-Olmo, M. Faúndez-Zanuy, K. L. De Ipiña, L. Calvó-Perxas and O. Turró-Garriga, Kinematic and pressure features of handwriting and drawing: Preliminary results between patients with mild cognitive impairment, Alzheimer disease and healthy controls, *Curr. Alzheimer Res.* **14**(9) (2017) 960–968.
31. M. T. Angelillo, F. Balducci, D. Impedovo, G. Pirlo and G. Vessio, Attentional pattern classification for automatic dementia detection, *IEEE Access* **7** (2019) 57706–57716.
32. R. Saha, A. Mukherjee, A. Sadhukhan, A. Roy and M. De, Handwriting analysis for early detection of Alzheimer's disease, in *Intelligent Data Analysis: From Data Gathering to Data Comprehension* (Wiley, 2020), pp. 369–385.
33. C. Taleb, L. Likforman-Sulem, C. Mokbel and M. Khachab, Detection of Parkinson's disease from handwriting using deep learning: A comparative study, *Evol. Intell.* (2020), pp. 1813–1824.
34. J. J. M. van Hoof, W. Hulstijn, H. van Mier and M. Pagen, Figure drawing and psychomotor retardation: preliminary report, *J. Affec. Disord.* **29**(4) (1993) 263–266.
35. B. Sabbe, W. Hulstijn, J. Van Hoof and F. Zitman, Fine motor retardation and depression, *J. Psychiatr. Res.* **30**(4) (1996) 295–306.
36. B. Sabbe, W. Hulstijn, J. van Hoof, H. G. Tuynman-Qua and F. Zitman, Retardation in depression: Assessment by means of simple motor tasks, *J. Affec. Disord.* **55**(1) (1999) 39–44.
37. R. Mergl, G. Juckel, J. Rihl, V. Henkel, M. Karner, P. Tigges, A. Schröter and U. Hegerl, Kinematical analysis of handwriting movements in depressed patients, *Acta Psychiatr. Scand.* **109**(5) (2004) 383–391.
38. S. Rosenblum, P. Werner, T. Dekel, I. Gurevitz and J. Heinik, Handwriting process variables among elderly people with mild major depressive disorder: A preliminary study, *Aging Clin. Exp. Res.* **22**(2) (2010) 141–147.
39. J. Heinik, P. Werner, T. Dekel, I. Gurevitz and S. Rosenblum, Computerized kinematic analysis of the clock drawing task in elderly people with mild major depressive disorder: An exploratory study, *Int. Psychogeriatr.* **22**(3) (2010) 479–488.
40. M. Freedman, L. Leach, E. Kaplan, G. Winocur, K. I. Shulman and D. Delis, *Clock Drawing: A Neuropsychological Analysis* (Oxford University Press, New York, 1994).

41. B. Gawda, Little evidence for the graphical markers of depression, *Percept. Mot. Skills* **117**(1) (2013) 304–318, doi: 10.2466/03.10.pms.117x15z8.
42. M. Giannini, P. Pellegrini, A. Gori and Y. Loscalzo, Is graphology useful in assessing major depression?, *Psychol. Rep.* **122**(2) (2018) 398–410.
43. J. Singh and M. A. Hamid, Cognitive computing in mental healthcare: A review of methods and technologies for detection of mental disorders, *Cogn. Comput.* **14**(6) (2022) 2169–2186.
44. Y. B. Ayzeren, M. Erbilek and E. Çelebi, Emotional state prediction from online handwriting and signature biometrics, *IEEE Access* **7** (2019) 164759–164774.
45. S. V. Kedar and S. Rokade, Recognition of emotional state based on handwriting analysis and psychological assessment, *Int. J. Eng. Adv. Technol.* **8**(6) (2019) 4395–4402.
46. J. A. Nolazco-Flores, M. Faundez-Zanuy, O. A. Velázquez-Flores, G. Cordasco and A. Esposito, Emotional state recognition performance improvement on a handwriting and drawing task, *IEEE Access* **9** (2021) 28496–28504.
47. J. A. Nolazco-Flores, M. Faundez-Zanuy, O. A. Velázquez-Flores, C. Del-Valle-Soto, G. Cordasco and A. Esposito, Mood state detection in handwritten tasks using PCA–MFCBF and automated machine learning, *Sensors* **22**(4) (2022) 1686.
48. G. Cordasco, F. Scibelli, M. Faundez-Zanuy, L. Likforman-Sulem and A. Esposito, Handwriting and drawing features for detecting negative moods, in *Quantifying and Processing Biomedical and Behavioral Signals*, eds. A. Esposito, M. Faundez-Zanuy, F. Morabito and E. Pasero (Springer, Cham, 2017), pp. 73–85.
49. G. Cordasco, M. Buonanno, M. Faundez-Zanuy, M. T. Riviello, L. Likforman-Sulem and A. Esposito, Gender identification through handwriting: An online approach, in *Proc. 11th IEEE Int. Conf. Cognitive Infocommunications (CogInfoCom)* (IEEE, 2020), pp. 197–202.
50. E. Sesa-Nogueras, M. Faundez-Zanuy and J. Mekyska, An information analysis of in-air and on-surface trajectories in online handwriting, *Cogn. Comput.* **4** (2012) 195–205.
51. P. F. Lovibond and S. H. Lovibond, The structure of negative emotional states: Comparison of the depression anxiety stress scales (DASS) with the Beck depression and anxiety inventories, *Behav. Res. Ther.* **33**(3) (1995) 335–343.
52. A. T. Beck, R. A. Steer, R. Ball and W. F. Ranieri, Comparison of Beck depression inventories-IA and-II in psychiatric outpatients, *J. Pers. Assess.* **67**(3) (1996) 588–597.
53. S. D. Østergaard, S. O. W. Jensen and P. Bech, The heterogeneity of the depressive syndrome: When numbers get serious, *Acta Psychiatr. Scand.* **124**(6) (2011) 495–496.
54. D. K. Ahorsu and H. W. Tsang, Do people with depression always have decreased cognitive processing speed? Evidence through electrophysiological lens, *Neuropsychiatry* **8**(4) (2018) 1227–1231.
55. M. Roca, M. Vives, E. López-Navarro, J. García-Campayo and M. Gili, Cognitive impairments and depression: A critical review, *Actas. Esp. Psiquiatr.* **43**(5) (2015) 187–193.
56. L. H. Dinehart, Handwriting in early childhood education: Current research and future implications, *J. Early Child. Lit.* **15**(1) (2014) 97–118.
57. K. H. James, The importance of handwriting experience on the development of the literate brain, *Curr. Dir. Psychol. Sci.* **26**(6) (2017) 502–508.
58. A. Agius, M. Morelato, S. Moret, S. Chadwick, K. Jones, R. Epple, J. Brown and C. Roux, Using handwriting to infer a writer's country of origin for forensic intelligence purposes, *Forensic Sci. Int.* **282** (2018) 144–156.
59. L. Gannetion, K. Y. Wong, P. Y. Lim, C. H. Chang and A. F. L. Abdullah, An exploratory study on the handwritten allographic features of multi-ethnic population with different educational backgrounds, *PLOS ONE* **17**(10) (2022) e0268756.
60. D. Sabic, A. Sabic and A. Bacic-Becirovic, Major depressive disorder and difference between genders, *Mater. Sociomed.* **33** (2021) 105–108.
61. M. Faundez-Zanuy and J. Mekyska, Analysis of gender differences in online handwriting signals for enhancing e-Health and e-Security applications, *Cognit. Comput.* **15**(1) (2023) 208–219.
62. S. Aleem, N. ul Huda, R. Amin, S. Khalid, S. S. Alshamrani and A. Alshehri, Machine learning algorithms for depression: Diagnosis, insights, and research directions, *Electronics* **11**(7) (2022) 1111.
63. G. B. Martins, J. P. Papa and H. Adeli, Deep learning techniques for recommender systems based on collaborative filtering, *Expert Syst.* **37**(6) (2020) e12647.
64. T. Hu, L. Xie, L. Zhang, G. Li and Z. Yi, Deep multimodal neural network based on data-feature fusion for patient-specific quality assurance, *Int. J. Neural Syst.* **32**(1) (2022) 2150055.
65. N. Kiriakidou and C. Diou, Integrating nearest neighbors with neural network models for treatment effect estimation, *Int. J. Neural Syst.* **33**(7) (2023) 2350036.
66. M. S. Shahabi, A. Shalbaf, B. Nobakhsh, R. Rostami and R. Kazemi, Attention-based convolutional recurrent deep neural networks for the prediction of response to repetitive transcranial magnetic stimulation for major depressive disorder, *Int. J. Neural Syst.* **33**(2) (2023) 2350007.
67. S. Zhang, H. Wang, Z. Zheng, T. Li, W. Li and Z. Zhang, Multi-view graph contrastive learning via adaptive channel optimization for depression

detection in EEG signals, *Int. J. Neural Syst.* **33**(11) (2023) 2350055.

68. C. Jiménez-Mesa *et al.*, Using explainable artificial intelligence in the clock drawing test to reveal the cognitive impairment pattern, *Int. J. Neural Syst.* **33**(4) (2023) 2350015.
69. Y. Dai, D. Qiu, W. Yang, S. Dong and H. Wang, Research on computer-aided diagnosis of Alzheimer's disease based on heterogeneous medical data fusion, *Int. J. Pattern Recognit. Artif. Intell.* **33**(5) (2019) 1957001.
70. D. Castillo-Barnes *et al.*, Nonlinear weighting ensemble learning model to diagnose Parkinson's disease using multimodal data, *Int. J. Neural Syst.* **33**(8) (2023) 2350041.
71. H. S. Nogay and H. Adeli, Machine learning (ML) for the diagnosis of autism spectrum disorder (ASD) Using brain imaging, *Rev. Neurosci.* **31**(8) (2020) 825–841.
72. H. S. Nogay and H. Adeli, Diagnosis of autism spectrum disorder based on structural brain MRI images using grid search optimization, and convolutional neural networks, *Biomed. Signal Process. Control* **79** (2023) 104234.
73. H. S. Nogay and H. Adeli, Detection of epileptic seizure using pre-trained deep convolutional neural network and transfer learning, *Eur. Neurol.* **83**(6) (2020) 602–614.
74. A. Bhattacharya, T. Baweja and S. P. K. Karri, Epileptic seizure prediction using deep transformer model, *Int. J. Neural Syst.* **32**(2) (2022) 2250058.